CORRELATION OF CLINICAL, RADIOLOGICAL, MICROBIOLOGICAL FEATURES AND DRUG RESISTANCE PATTERN OF MYCOBACTERIUM TUBERCULOSIS IN PATIENTS WITH HIV TUBERCULOSIS CO-INFECTION

Dissertation submitted In Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF MEDICINE
TUBERCULOSIS & RESPIRATORY DISEASES
Branch - XVII
2012-2015

DEPARTMENT OF TUBERCULOSIS & RESPIRATORY DISEASES
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APRIL 2015

CERTIFICATE

This is to certify that the dissertation on **"CORRELATION OF CLINICAL, RADIOLOGICAL, MICROBIOLOGICAL FEATURES AND DRUG RESISTANCE PATTERN OF MYCOBACTERIUM TUBERCULOSIS IN PATIENTS WITH HIV TUBERCULOSIS CO-INFECTION"** is a record of research work done by **DR.V.ELAKYA** in partial fulfilment for M.D.(PULMONARY MEDICINE) Examination of the Tamilnadu, Dr.M.G.R.Medical University to be held in April 2015.The period of study is from April 2013 to March 2014.

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DECLARATION

I hereby declare that the dissertation entitled **"CORRELATION OF CLINICAL, RADIOLOGICAL, MICROBIOLOGICAL FEATURES AND DRUG RESISTANCE PATTERN OF MYCOBACTERIUM TUBERCULOSIS IN PATIENTS WITH HIV TUBERCULOSIS CO-INFECTION"** submitted for the Degree of Doctor of Medicine in M.D., Degree Examination, Branch VII, PULMONARY MEDICINE is my original work and the dissertation has not formed the basis for the award of any degree, diploma, associate ship, fellowship or similar other titles. It had not been submitted to any other university or Institution for the award of any degree or diploma.

Place: Chennai Signature of the Scholar

Date : 09.2014

(Dr.V.ELAKYA)

ACKNOWLEDGEMENT

Language with all elaborations seems to be having limitation especially when it comes to expression of feelings. It is incapable of conveying in words all the emotions and feelings one wants to say.

It would take pages to acknowledge everyone who, in one way or another has provided me with assistance, but certain individuals deserve citation for their invaluable help.

I would like to express my heartful thanks to the **Prof.Dr.AL.Meenakshi Sundaram, M.D,** Dean, Stanley Medical College and Hospital for giving me permission to conduct this study.

I find words insufficient to express my deep sense of gratitude for my esteemed and reverend teacher, my chief **Prof.Dr.C.Chandrasekar M.D, D.T.C.D,** Head of Department, Dept. of Pulmonary Medicine, Stanley Medical College and Superintendent, Govt. Hospital of Thoracic Medicine, Tambaram Sanatorium, for his ever-inspiring guidance and personal supervision. The finest privilege in my professional career has been the opportunity to work under his inspirational guidance.

I thank Associate professor **Dr.O.R.Krishnarajasekhar M.D, D.T.C.D** for his constant encouragement and guidance throughout my postgraduate course.

I am very grateful to Associate professor **Dr.R.Sridhar M.D, D.T.C.D** for providing valuable assistance and timely advice. He has never hesitated in providing support whenever I needed throughout my work.

I would like to express my sincere thanks and heartful gratitude to Assistant professor **Dr.Allwyn Vijay M.D,** for his constant support, enthusiasm and valuable guidance throughout my work.

Words fall short in expressing my sincere gratitude for other eminent teachers in our department, who helped me in my work; **Dr.N.Ravichandran M.D, Dr.S.Kumar M.D, Dr.Raja M.D, Dr.S.P.Vengada Krishnaraj.** My work would have been incomplete without their support. I express my sincere thanks to all the assistants in our department for their support.

I have no words to express my sincere and heartful gratitude to my father **Mr.D.Vanavil** and my mother **Mrs.Vasugi** who always supported me throughout my life as a student, guided me to solve my

problems and helped me to face all kind of challenges. Their love, affection and support enabled me to reach this stage of life.

I will always be grateful to my dear husband **Dr.C.Arul Murugan M.D** for being co-operative, for sharing my enthusiasm and dismay and constantly supporting my ambitions and struggle. This work would not have been possible without his support in my difficult times.

Last but not the least , I thank all the patients who cooperated with me throughout my work.

Finally it is endowment of spiritualism and remembrance of ALMIGHTY for all that I achieved.

CONTENTS

ABSTRACT

CORRELATION OF CLINICAL, RADIOLOGICAL, MICROBIOLOGICAL FEATURES AND DRUG RESISTANCE PATTERN OF MYCOBACTERIUM TUBERCULOSIS IN PATIENTS WITH HIV TUBERCULOSIS CO-INFECTION

INTRODUCTION

Drug Resistant Tuberculosis is a major challenge in tuberculosis high prevalent countries. This challenge becomes bigger where HIV TB coinfection is present. 24.6% of TB deaths occur among HIV positive cases.

AIM

To determine the correlation between clinical, radiological, microbiological features and the drug resistance pattern of Mycobacterium tuberculosis in patients with HIV tuberculosis co infection.

OBJECTIVES

1. To determine the relationship between clinical presentation of HIV - pulmonary tuberculosis co infection and drug resistance pattern.
2. Compare each of the variables CD4 count, HIV staging, chest Xray features, sputum smear for AFB, LPA with drug resistance pattern.
3. Prevalence of MDR-TB in HIV TB co-infection.

MATERIALS & METHODS

It is a prospective study done at Government Hospital of Thoracic medicine, during April 2013 to March 2014.

Inclusion Criteria : All HIV seropositive patients with pulmonary TB, Age > 18 years

Exclusion Criteria: HIV patients with only extrapulmonary TB, Age < 18 years, Patients who are moribund, sick and unable to produce sputum, Patients who are not willing to participate in the study, Patients whose sputum showed no growth in LJ culture medium.

Collection of clinical samples/ data: Symptoms duration, HIV diagnosis and treatment history, Antituberculous treatment history, Height & Weight, Chest radiograph, Sputum for AFB staining, LPA, sputum Mtb culture, CD4 count. Allotting score for each of the variable. Predict MDR based on score. Comparing prediction with sensitivity results and analyse.

Features/score	0	1	2
Contact H/o PT	absent		present
H/O ATT	No		Yes
HIV STAGE 4	No	Yes	
CD4 count	>200	<200	
BMI	>18	<18	
Pulmonary TB	alone	with dissemination	
chest xray	no cavity	cavitation	
sputum smear	negative	positive	

OBSERVATION & RESULTS

230 patients were included in the study - 198 were male, 32 female. Mean age 39.5. totally 5.2% cases were MDR, 4.8% monoresistant to Rifampicin (R). Among new case, MDR 3.4%, monoresistants to R 2.7%. Among retreatment cases, MDR was 8.5% and monoresistant to R 8.5%. Odds ratio was 3.18 (95% CI 1.31 - 7.71) when Rif resistance is compared with TB case. 10% of disseminated TB cases are MDR. Association between disseminated TB & Rif

Resistance is odds ratio of 2.71 (95% CI 1.07 – 6.09) P value of 0.56 (> 0.05) is obtained when symptoms duration is compared with rifampicin resistance. CD_4 count compared with MDR - TB gives odds ratio of 7.30 (95% CI 0.92 – 57.71). Odds ratio is 2.59 (95% CI 1.08 – 6.03) where HIV stage is compared with rifampicin resistance. Drug sensitivity of 154 cases were obtained by LPA, rest were obtained by culture. 67% of MDR cases were detected using LPA. Odd's ratio is 2.96 (95% CI 1.23 – 7.12) when score more than 4 compared with Rifampicin resistance.

CONCLUSION

In summary, prevalence of MDR TB in this study is 2.2% in new cases and 8.5% in retreatment cases. Prevalence of Rifampicin resistance in new cases is 6.1% and that in retreatment cases is 19%.

History of prior treatment of tuberculosis, HIV stage 4, disseminated TB were significantly associated with rifampicin resistance.

In this study, *CD4 count less than 200* was significantly associated with MDR TB and drug resistant TB.

HIV treatment was not associated with drug resistance pattern. Duration of symptoms did not affect prevalence of MDR TB. There was no significant association between chest x ray lesions, cavitation with MDR TB. Sputum smear status had no significant relation with MDR TB.

Sensitivity of line probe assay in this study is 67%.

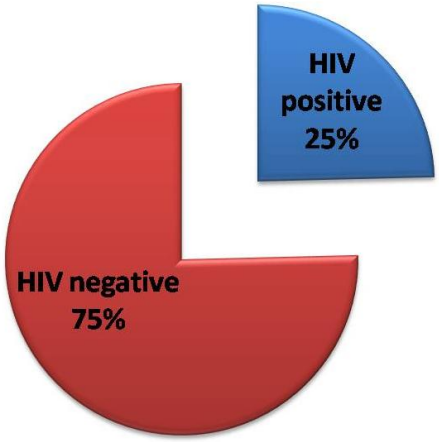
Scoring with 8 variables with score more than 4 was significantly associated with Rifampicin resistance. Since the study population is small, further studies with large study population will be helpful in validating this score.

Keywords

HIV, Tuberculosis, Drug Resistance, Line Probe Assay.

INTRODUCTION

Drug resistant tuberculosis is the biggest challenge in tuberculosis high prevalent countries. In 2012, there were an approximately 8.6 million incident tuberculosis(TB) cases and 1.3 million people lost their lives due to the disease[1]. Among these 1.3 million deaths, 3,20,000 were among people who were human immunodeficiency virus (HIV) positive[1]. Thus 24.6% of TB deaths occurred among HIV positive cases.



TB deaths in world

Among these deaths, 1,70,000 deaths were due to multidrug resistant tuberculosis(MDR TB). Thus 13% of deaths is due to MDR TB globally[1]. This is relatively high when compared with 4,50,000 incident cases of MDR TB annually.

Indian Scenario

In 2012, there was an estimated 2.2 million incident TB cases in India[1]. This shows that India has the lion's share of global TB cases amounting to 26% of total cases.

3,10,000 people died due to TB in India in 2012[1]. 42,000 deaths among these occurred in HIV positive individuals. Estimated prevalence of HIV among TB patients in India is 5.95%[3].

Drug Resistance Surveillance studies have estimated the prevalence of MDR-TB to be about 2.2% in new cases and 15% in re-treatment cases[1].

HIV-TB co infection is another massive challenge to TB control in resource limited countries. There exists a synergetic relationship between tuberculosis (TB) infection andHIV infection which results in arise in their prevalence, morbidity and mortality[2]. This co-infection is a huge public health problem that is ominous as a potential pandemic. This should be of serious concern and spur emergency action to control and reduce these infections.

The interaction between TB and HIV is as follows:

In HIV:

• TB is a most important co-infection[2];

• TB infects both HIV-infected and non-infected persons;

• TB is the leading cause of mortality in HIV patients[2];

• TB causes serious illness and accelerates progression to AIDS.

In TB:

• HIV is the main risk factor for progression from latent TB infection to active disease[2];

•HIV increases the risk of recurrent TB[2].

• HIV leads to increase in TB incidence;

• HIV gives rise to hot spots of TB transmission[2];

• HIV causes increase in morbidity in TB patients because of HIVrelateddiseases[2];

• HIV elevates the adverse drug reactions to TB treatment[2];

• HIV raises TB case fatality rates;

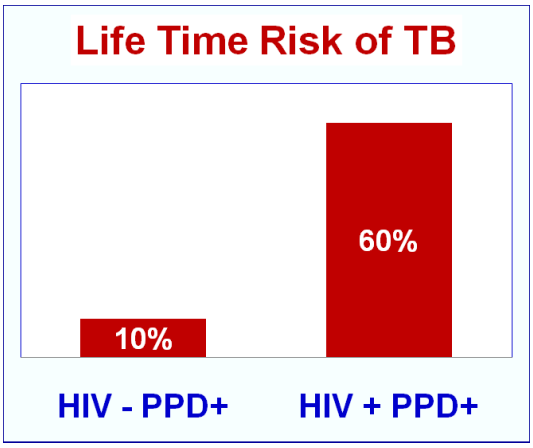
As the patient becomes severely immunosuppressed with the advancement of disease, the presentation is more likely to be extra-pulmonary or smear-negative than in HIV-uninfected TB patients[4]. This faces a major challenge in diagnosis and result in misdiagnosis or delays in diagnosis[4], and therefore, higher morbidity and mortality due to HIV

TB co-infection. In such scenarios, when diagnosing TB becomes difficult, diagnosing drug resistant TB becomes much more difficult. This study helps in identifying predictors of MDR TB in HIV patients, thus helping in early diagnosis of MDR TB in HIV patients.

REVIEW OF LITERATURE

Risk of TB in HIV patients

HIV patients have increased risk of acquiring tuberculosis. Life time risk of tuberculosis in non HIV individuals with latent TB infection is 10%.For HIV-infected individuals with latent TB infection, the annual risk of developing active TB reaches 5–10%[6] and lifetime risk increases to 60%.



HIV patients are more prone to

- Develop active TB, once infected.
- Relapse TB after completing treatment.
- Acquire re-infection with another strain of TB bacilli
- Increased mortality

Prevalence of HIV in TB patients in India is 5.95%[3].

Pathogenesis of TB

The pathogenesis of tuberculosis depends on the cellular immunity of the host. This cellular immunity is responsible for the resistance to bacteria and also for the hypersensitivity to tubercular antigens[7]. Alveolar macrophages are the primary cells infected by the bacilli. During early phase of infection, bacilli proliferate in macrophages and during late phase, macrophages are stimulated by T_h1 response to contain the infection.

TB bacilli enter macrophages by endocytosis, by binding to mannose receptors[7]. Mycobacteria multiply within the macrophages by blocking phagolysosome formation. Several mechanisms involved in this are inhibition of calcium channels and blocking assembly of proteins required for phagosome and lysosome fusion. Bacilli enter the blood stream and seeding at multiple sites occurs. Patient is asymptomatic at this stage.

After 3 weeks, antigen presenting cells in the lymph nodes, are activated by mycobacterial antigens. These cells stimulate T_h1 cells by releasing IL-12. Mature T_h1 cells in lungs and node produce Interferon – gamma[7] (IFN –γ). IFN –γ plays a major role in activating macrophages by stimulating the formation of phagolysosome. Phagolysosome creates

an acidic environment which is inhospitable to bacilli. IFN –γ stimulates macrophages to release iNOS[7]. iNOS releases nitric oxide. Nitric oxide releases reactive nitrogen species and also promotes release of oxygen free radicals. These free radicals promote destruction of mycobacterial constituents.

IFN –γ plays main role in formation of granuloma. IFN –γ activates macrophages. They release tumor necrosis factor (TNF). TNF recruits monocytes which differentiate into epitheloid histiocytes[7]. Epitheloid cells helps in the formation of granuloma. This characteristic granuloma formation is absent in HIV patients.

T_h1 cells has major role in containing the disease. Any defect in T_h1 response, thus leads to absence of resistance and disease progression.

TB Reactivation by HIV

The depletion of CD4+T cells is a significant contributor to the increased risk of reactivation of latent TB and susceptibility to new M. tuberculosisinfection[6]. CD8+T cells have a role in the control of latent TB[6]. M. tuberculosis infection is rampant in patients with HIV are due to deregulated chemotaxis, HIV manipulation of macrophage bactericidal pathways[8], up-regulation of M. tuberculosis entry receptors

on macrophages[9] , and a tipped Th1/Th2 balance . HIV attenuates tumor necrosis factor (TNF)-mediated macrophage apoptotic response to M. tuberculosis and thus promotes bacterialsurvival[10].

An alteration of the level of the protective adaptive immune responses facilitates reactivation of TB infection[8]. Several immune mechanisms, such as increased production of IL-27[11], TGF-b , PGE-2, SOCS1, or the decoy receptor D6 or decreased levels of TNF, IFN-c, and polyfunctional specific T cells, are considered to play a significant role in such reactivation[8]. Factors like IL-27down-regulate the IFN-c/IL-12 axis thus weakening bacterial control[8]. D6 decoy receptor suppress efficient bacterial clearance.

Granulomas are the hallmark of TB's pathology. Mycobacteria are contained in the granuloma, which localizes infection and thus efficiently preventing dissemination of the bacilli between hosts[8]. This contributes to protection. TNFandCD4+cells are imperative in preserving granuloma organization. Formation of granuloma may fail in people with immunocompromised state. TB patients with AIDS have a dominant granulocytic infiltrate and necrosis[8]. They are devoid of the caseous necrosis present in non-HIV-infected patients with TB granulomas[8]. This is due to depletion of CD4+cells in the granuloma. This leads to a direct disruption of structure of granuloma and

obliteration of the containment of bacilli. In HIV-infected patients it can be a disseminated disease affecting multiple organs that are devoid of well-definedgranulomas[8]. All types of extrapulmonary TB have been reported in HIV infected patients.

Features of Immune Response to HIV Infection

The depletion of CD4+T cells is the hallmark of HIV infection[8]. Various factors are implicated in progression of HIV disease :

- Depletion of the effector memory CD4+T cells present in the gut mucosa[8].
- Depletion of CD4+ cells.
- Systemic and chronic state of immune activation[8]
- Accelerated T cell turnover
- Hyper-responsiveness of plasmacytoid DCs during the initial infection[8]
- Increased gut permeability causing microbial translocation.

T cell immunoglobulin mucin 3 (Tim-3) and Programmed Death 1 (PD-1) are few of the markers of T cell exhaustion in HIV-1+patients[8]. They are released by constant antigenic stimulation. Both molecules promote the down regulation of host immune responses[8]. They help in sustaining T cell tolerance. Tim-3 is up-regulated in virus-specific CD8+T cells in chronic progressive HIV infected patients[14]; Tim-3 is

up-regulated in antigen-specific CD8+Tcells in patients suffering from active TB[15]. This indicates that similar inhibitory receptor/ligand interactions play a major role in regulating host immunity to both M. tuberculosis and HIV infections in humans.

Manifestations of TB in HIV patients

TB presentation in HIV patients differs depending on the level of immunosuppression.

Early phase of immunosuppression

- Tuberculosis presents as post primary TB
- Sputum smear is positive for Acid fast bacilli[18].
- Chest x-ray often shows cavities.

Late phase of immunosuppression

- Usually resembles primary TB
- Usually smear negative
- Chest x-ray shows atypical presentations like mid and lower lung field lesions, infrequent cavities, intra thoracic lymph nodes.
- Mycobacteremia and extrapulmonary tuberculosis.

% of Sputum smear positivity in pulmonary tuberculosis

- HIV negative – 60%
- Early HIV - 50 %
- Late HIV - 30%

- In early phase of Immunosuppression, cavities are part of manifestations of pulmonary TB and so 50% of patients will have Sputum Smear positive results. However, inHIV patients sputum smear positivity rate will be less, compared with HIVnegative patients.
- In late phase, though there is increased bacterial load, sputum smear negativity is frequent . This is due the absence of bronchial wall destruction because of reduced T cell mediated hypersensitivity resulting in expectoration of fewer bacilli in sputum[7]. Cavity formationis also less frequent.

Mycobacteremia in HIV

Mycobacteremia is presence of mycobacteria in blood stream. This occurs when CD4 count falls below 200. This is because of fall in immunity leading to breakdown of granuloma that had contained the bacilli in localized sites. Moreover granuloma formation is affected when the immunity is lowered. This leads to spread of bacilli in blood to various sites. It causes seeding of bacilli in various organs which then manifests as disseminated TB and extrapulmonary TB.

The extent of immunosuppression determines the frequency of extrapulmonary involvement[7]. Frequency is 10 to 15% in mildly immunosuppressed[7] cases whereas it raises to an alarming 50% in severely immunosuppressed individuals.

Extrapulmonary sites frequently affected are lymph nodes, central nervous system (meningeal and parenchymal), bone marrow, soft tissue, liver and other visceral organs.

Lymphadenopathy is a common presentation in HIV cases[19]. It may be due to various causes like primary HIV adenopathy, TB lymphadenitis, Non tuberculous mycobacteria, nodal lymphoma, nodal Kaposi Sarcoma. It is more common in males in HIV positive cases. In addition to cervical nodes, there is increased incidence of axillary and inguinal nodes in HIV patients when compared to HIV negative cases. In HIV negative cases, nodes are usually unifocal and they do not have extranodal disease. Frequency of multiple site involvement is more in HIV patients. Granuloma formation is less in these nodes[19]. They are more prone to suppuration and abscess formation. In contrary to sputum which is paucibacillary, pus from these abscess usually contain plenty of bacilli. Nodal TB can also present as a manifestation of Immune reconstitution inflammatory syndrome.

HIV patients are at an increased risk of developing central nervous system tuberculosis including tuberculous meningitis and tuberculoma[19]. The presentation, CSF findings of TB meningitis are usually similar to that in HIV seronegative patients. But sometimes CSF findings can be normal. In such cases radiographic findings come to aid in diagnosis of TB meningitis. They are cisternal enhancement, basal ganglia infarction, multiloculated abscesses and communicating hydrocephalus[19]. Extrameningeal TB is also more common in HIV cases. Tuberculoma is seen in 50% of cases with TB meningitis. Neurological tuberculosis has been initial presentation in a quite a number of few cases.

Several hematological manifestations are seen in HIV TB co-infected cases. This is mainly due to bone marrow infiltration. Granulomas are present in bone marrow. They are different from classic granuloma as they are surrounded by polmorphonuclear cells and macrophages instead of lymphocytes. These granulomas have abundant bacilli. In many cases bone marrow aspirate has helped in diagnosing TB in high prevalent countries like India.

Exacerbation of HIV Infection by M. tuberculosis infection

The mortality and incidence rates are higher for new AIDS-defining opportunistic infections if the individuals are co-infected with HIV &TB. M.tuberculosis infection has a negative effect on the immune response to HIV and on progression to AIDS[8].HIV and TB bacilli, both modulates the action of macrophages and dendritic cells. Replication of HIV is increased locally at sites which are affected by TB bacilli in lungs, pleura and lymph nodes. M.tuberculosis up-regulates HIV replication in acutely and chronically infected T cells or macrophages, and also ex vivo in alveolar macrophages and lymphocytes from HIV patients[16,17]. These findings are also substantiated in real time because plasma viral loads are increased in HIV patients when they are suffering from active tuberculosis.

***Clinical screening algorithms*:**

The WHO recommends that screening for TB should be done at the time of diagnosis of HIV in patients. Screening must also be done before starting antiretroviral therapy and during follow up.

In 2007, WHO released new guidelines to help in the diagnosis of TB in HIV infected individuals[20]. This committee recommended that screening for TB must include asking questions about a group of symptoms like presence of current cough, night sweats, fever or weight

loss rather than chronic cough alone[6]. Sensitivity of this rule was shown to be 79 per cent with 50 per cent specificity. Sensitivity was 90% in clinical settings. The main change to existing practice will be the replacement of chronic cough by current cough as screening question and also adding of other symptoms to routine screening[20]. This screening tool can be used in ART centres to identify TB patients[20]. They must be subjected to further investigations for confirming the disease.

Radiographic findings:

Chest xray when used along with symptoms helps in identifying more number of TB cases. But a normal chest x-ray does not rule out the possibility of TB in HIV patients because upto 14% of patients may have normal xray. These patients can be identified using nucleic acid amplification tests orsputum culture for diagnosingTB.

Sputum smear microscopy:

Microscopic examination ofsputum for acid-fast bacilli (AFB) is most commoly used for diagnosing TB. They are cheap, easy to perform and mostly specific. For a specimen to be smear positive, it must contain approximately 10^5bacilli permilliliter[22]. Sensitivity of sputum microscopy in HIV cases varies from 43 to 51 per cent[21].Techniques that

boost the sensitivity are fluorescence microscopy, specimen processing methods, like concentration, bleach sedimentation and same-day sputum collection methods[23-25]. Light-emitting diode(LED) bulbs reduce the cost of fluorescence microscopes. This helps in widespread use of fluorescent microscopes.

However, in resource limited settings, only sputum smear examination is routinely done for screening TB. This leads to delay in diagnosis of smear negative pulmonary TB cases in HIV patients. The drug susceptibility cannot be found by smear microscopy is also a major drawback.

Growth based detection:

Culture of *Mycobacterium tuberculosis* is more sensitive than sputum smear. It is recommended to help in the diagnosis of TB in HIV-infected cases[26].Culture can be used for strain characterization or drug susceptibility testing. The solid medium like the Lowenstein-Jenson (L-J) medium is slow, because growth of culture takes 6-8 weeks[20]. This leads to delayed initiation of treatment, which leads to adverse outcome of HIV TB co-infected individuals. Liquid culture mediums detect growth of mycobacteria in less than 1-2wk by fluorescent sensors [BACTEC Mycobacteria Growth Indicator Tube 960];bacterial carbon

dioxide production or oxygen consumption with radiometric sensors (BACTEC 460TB)[20].

Microscopic observation drug susceptibility (MODS)

It is used for detection of microcolonies, cord formation and also for early detection of drug resistance[20].It has higher sensitivity, less time to culture positivity.

Molecular techniques:

Nucleic acid amplification testing (NAAT) has high specificity, but its sensitivity is variable. Simplified versions of NAAT kits include fluorescence *in-situ* hybridization (FISH) loop-mediated isothermal amplification (LAMP) and line probe assays (LPA).

LPA has high sensitivity (>95%) and specificity (100%) when culture isolates were used[27]. It detects both *M. tuberculosis* complex as well as isoniazid resistance[28] by inh gene, katG gene and rifampicin resistance by rpoB gene from early positive growth on culture or on smear-positive sputum. Processing by LPA involves four steps. First, bacterial DNA is extracted from the specimen. Second, resistance determining genes are amplified by polymerase chain reactions (PCR) using specific primers. Third, these products from PCR are hybridized with oligonucleotide probes (that are immobilized on a strip). Finally,

the captured labeled hybrids are detected using colorimeter. Results obtained within 48 – 72 hours.

GeneXpert-Rif:

WHO has endorsed the use of GeneXpert-Rif for the rapid diagnosis of TB as well as rifampicin resistance among HIV-infected patients with clinical suspicion of TB[29]. It is a TB-specific automated, cartridge-based nucleic acid amplification assay, which has fully automated and integrated sample preparation, amplification and detection using real-time PCR. It provides results within100 minutes. Sensitivity of a single Xpert MTB/RIF test in smear-negative/culture positive patients was 72.5 per cent which increased to90.2 per cent when three samples were tested[20]. XpertMTB/RIF specificity was 99 per cent. Xpert MTB/RIF detected rifampicin resistance with 99.1% sensitivity and excluded resistance with 100 per cent specificity[30, 31]. This test has the potential to change the current reference standard of TB diagnostics[20].

Tuberculin skin test[20]:

Tuberculin skin test positivity provides evidence of TB infection. Many HIV infected patients have a negative skin test in spite of TB infection or disease, due to anergy.

Tuberculin skin test underestimates the prevalence of latent tuberculosis in endemic countries. The test is neither useful to rule in disease nor in high TB prevalence settings to identify eligible individuals for prophylaxis.

Other diagnostic techniques

(i). Interferon-γ release assay[20] (IGRA): This test is used to diagnose latent TB infection and is mainly useful in profoundly ill patients and those with severe malnutrition. There two *in vitro* tests to detect latent tuberculosis are: QuantiFERON- TB Gold and the T SPOT-TB test.

Both use an enzyme- linked immunospot assay to quantify the number of peripheral blood mononuclear cells producing IFN- γ in response to tuberculosis specific antigen stimulation (ESAT-6 and CFP10).They are more expensive. IFN-γ assays do not differentiate between latent and active tuberculosis or between immune reconstitution inflammatory syndrome (IRIS) and failure. WHO recommended against the use of IGRAs for diagnosis of active or latent TB, in resource limited settings.

(ii) Volatile organic compounds[20] (VOCs):

These compounds released by TB bacilli in urine or exhaled air over sputum or bacterial culture, are calculated using sensors or gas chromatography–mass spectroscopy. It has been identified that infection

with TB produces a distinct pattern of certain VOCs when compared to healthy individuals. Identification of these patterns helps in creating a portable “electronic nose” which could sniff urine samples rapidly to diagnose TB.

Management of HIV-TB co-infected patients

It includes various aspects of treating the patients

- Anti-TB drugs should be given
- Evaluation for other opportunistic infections to be done.
- Cotrimoxazole prophylaxis to be given to all cases HIV TB co-infection
- Appropriate nutrition ensured for all patients
- All family members to be screened for HIV and TB infection
- ART to be initiated for all cases of HIV TB co infection

HIV-TB: Anti TB Treatment

First line drugs used in management of tuberculosis are :

- isoniazid(H) ,
- Rifampicin (R) ,
- Pyrazinamide (Z) ,
- Ethambutol (E) ,
- Streptomycin(S)[4].

Isoniazid

It is a bactericidal drug. It acts both intracellularly and extracellularly.It is a prodrug. It acts by inhibiting cell wall synthesis. Resistance to isoniazid[32] occurs due to

- Overexpression of inhA
- Mutation/Deletion of KatG gene
- Promoter mutations
- Kas A mutation

Mutations causing resistance to isoniazid occurs in about *1 in* 10^6 replications[19].

Main adverse effects are hepatotoxicity and peripheral neuropathy. Other adverse effects are transient memory loss, seizures, psychosis, tinnitus, abdominal discomfort, gynaecomastia.

Daily dose is 5mg/kg. Thrice weekly dose is 10mg/kg.

Rifampicin

It is also a bactericidal drug.It acts both intracellularly and extracellularly. It acts on both slow dividing cells and actively dividing bacilli. It has sterilizing effect. It binds to beta subunit of DNA dependent RNA polymerase and inhibits DNA dependent RNA synthesis[32].

Resistance of rifampicin

- Mainly due to mutation in rpoB gene[32]. Mutations causing resistance to isoniazid occurs in about *1 in 10^8 replications*[19].

It shows cross resistance to rifabutin and rifapentine.

Major adverse effects are hepatotoxicity, respiratory syndrome, purpura, hemolysis, shock and renal failure. Minor reactions are, flu syndrome,cutaneous syndrome and abdominal syndrome, proteinuria, orange red urine, acute tubular necrosis[22].

Rifampicin resistance is strong correlator of MDR TB. Under RNTCP, those cases with rifampicin resistance are treated with Category IV ATT drugs[4].

Regimen for HIV TB co-infected cases[18]

Category of treatment[18]	Type of Patient	Regimen
New (Category I)	1. New sputum smear positive 2. New sputum smear negative 3. New extra pulmonary TB	$2H_3R_3Z_3E_3$ + $4H_3R_3$
Previously treated (Category II)	1. Sputum smear positive Relapse 2. Sputum smear positive Failure 3. Sputum smear positive Treatment after Default 4. Others	$2H_3R_3Z_3E_3S_3$ + $1H_3R_3Z_3E_3$ + $5H_3R_3E_3$

Outcome of Anti-TB Treatment

Outcome of TB Treatment in HIV patients without ART depends on CD4 Count during initiation of ATT. Immune status (CD4%) decelerates even when patient is on Anti TB treatment (without ART)[5]. It is associated with increased death rate because of HIV and other opportunistic infection. ATT without ART in HIV patients is associated with increase in relapses and re infections because of persistence of TB bacilli and low immune response.

CD4% count falls while under Anti TB treatment without ART.

Assessment	CD4 %	CD4 count (cells/mm^3)	Viral load (copies/ml)
0 month	13.8 ± 9	182 ± 144	$13x10^5$ ± $2.5x10^3$
End of Treatment	11 ± 9	186 ± 87	$3.8x10^5$ ± $5.6x10^3$
p value	< 0.001	NS	0.05

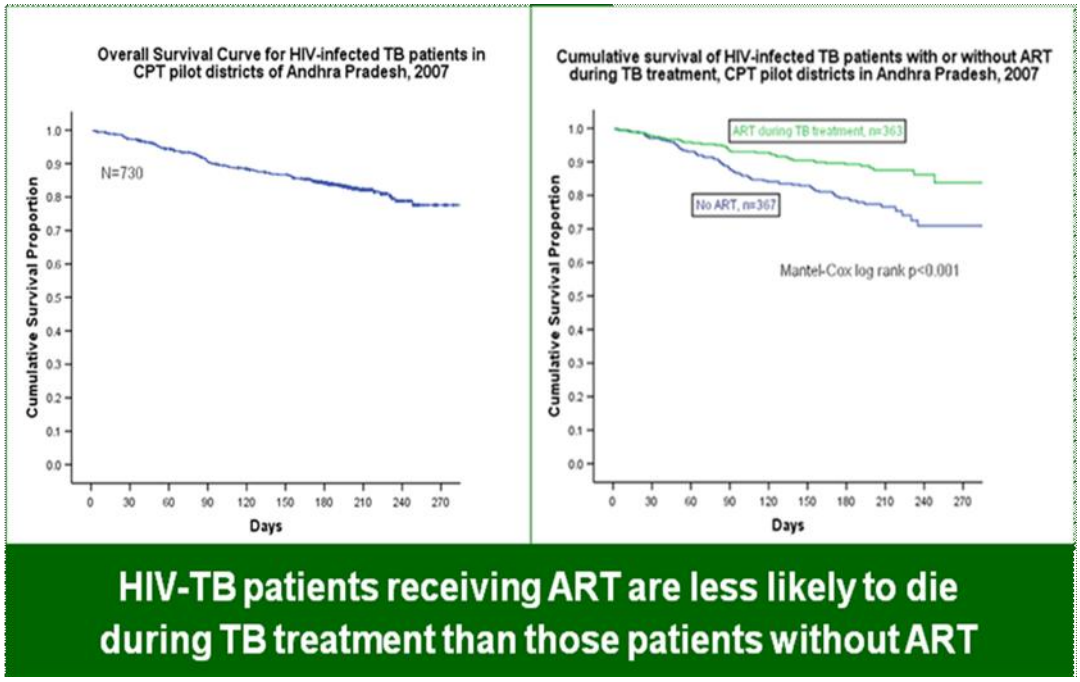
This table is from the pilot study by Swaminathan.S et al, which evaluated the efficacy of RNTCP Anti-TB treatment in HIV patients, in the year 2000, when National ART Programme has not come into force.

The study assessed the efficacy of RNTCP Anti-TB treatment in relation to the rise in Immune status (CD4 count and CD4%) and fall in the viral burden.It brings out an important quality assessment factor, demonstrating the considerable CD% decline, despite 6-months of supervised anti TB treatment, of course without ART. This explicitly underlines the significance of initiating ART also in those PLHIV patients with low CD4 counts.

Early ART	**Deferred ART**
Increase in cure rate, reduction in relapses	Drug interaction decreased
Early mortality due to TB is decreased.	Reduction in toxicity
Prevents other OI's concurrently	Decrease in IRIS
Period of Hospitalization minimized	ATT period can be used as a foundation for better adherence to ART
Drug resistance caused by malabsorption can be reduced	Management of ATT toxicity is crucial for subsequent ART adherence

This table compares the benefits of early versus deferred ART in HIV TB co-infected patients. While the dangers of IRIS and drug toxicities are present, the significant advantage of early ART is the considerable reduction in deaths.

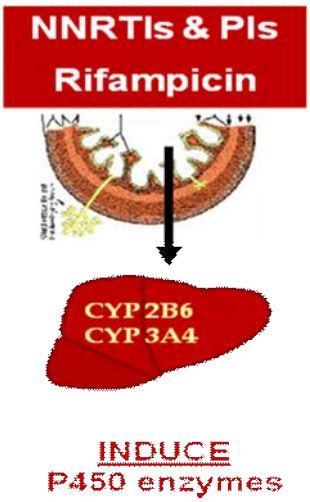
Role of ART in Reducing Mortality[5]



The graph on the left shows the overall survival rate of 730 HIV-TB co-infected patients which was 82% during TB treatment.

The graph on the right side shows the cumulative survival rate of 730 HIV TB co-infected cases with or without ART while on TB treatment. Among these cases, 363 HIV-infected TB patients were given ART also, had the survival rate of >88%. But, the survival rate of those 367 HIV-infected TB patients, who did not receive ART was found to be<75%. This undoubtedly establishes the need of ART with ATT in the treatment of HIV infected TB patients to decrease the mortality rate.

Drug Interactions between ART and ATT



- Rifampicin activates cytochrome P450 enzymes in the liver that metabolizes NNRTIs and PIs[5].
- Rifampicin notably reduces the bioavailability of Nevirapine and C min to sub-therapeutic levels in 62% of patients[5].
- Protease inhibitors and NNRTIs can enhance or inhibit this system leading to altered blood levels of many other drugs[5].

First Line Antiretroviral therapy for HIV-TB co-infection in India[5]

The following Antiretroviral therapy regimens are used in the management of HIV TB co infected patients in India.

ZIDOVUDINE OR + LAMIVUDINE + EFAVIRENZ[5] TENOFOVIR

The regimens used depend on the hemoglobin level of the patient.

Regimen II	Zidovudine + Lamivudine + Efavirenz	Preferred regimen, if patient's Hb ≥9gm/dl
Regimen II (a)	Tenofovir + Lamivudine + Efavirenz	Preferred regimen if patient's Hb <9 gm/dl

Initiation of ART in PLHIV with TB Co-infection

Type of Tuberculosis

Pulmonary TB (Stage III)

Extra pulmonary TB (Stage IV)

Eligible Clinical Staging

Initiate ART irrespective of clinical stage

Eligible CD4 Counts

Initiate ART irrespective of CD4 count

Timing of ART in accordance with start of TB treatment

- Start ATT first (Category I or II)
- Start ART as soon as TB treatment is tolerated[5]
- after 2 weeks & before 2 months

ART Regimen

Start Efavirenz containing ART Regimen

Patient should be monitored for toxicities associated with both ATT and ART.

ART after Anti TB Treatment

- Nevirapine containing regimen is used after completion of ATT[5].

- For a period of one week Nevirapine and Efavirenz are given together. Then Efavirenz is discontinued.
- Nevirapine is given in the dose of 200 mg bid
- The major adverse effect associated with introduction of Nevirapine is Steven Johnson syndrome, which may at times be lethal.

Immune Reconstitution Inflammatory Syndrome (IRIS): Tuberculosis

- Antiretroviral therapy suppresses the viral replication and thus boosts the immunity of the patient. When immunity is restored there is a rise in CD4 count . Since manifestations of TB is due to immune response, the boosted immunity mounts immune response against TB bacilli in the body leading to various manifestations like CNS TB , lymphadenopathy or worsening of lesions in lungs. This phenomenon is known as IRIS[19].
- There are two types of IRIS – unmasking or paradoxical reaction. Unmasking is occurrence of new lesions. Paradoxical reaction is worsening of existing symptoms. TB is the most common infection, manifesting as “IRIS”.

- Onset of symptoms is between 2 weeks and 2 months. It may occur even after one year in rare cases. Duration of symptoms is usually 3 weeks.

Second Line ART regimen for HIV-TB in India

Tenofovir +Lamivudine+Atazanavir/ritonavir [5]

- Second line regimen consists of two protease inhibitors in addition to first line drugs. Protease inhibitors are metabolized by Rifampicin and their blood levels are reduced. This leads to treatment failure.
- Rifampicin is avoided in these patients. Rifabutin is used instead of Rifampicin. Rifabutin has less enzyme inducing property, so interaction with protease inhibitors is also less.
- Dose of Rifabutin is 150mg, thrice a week.

Causes for Drug Resistant TB in HIV[18]

- It is mainly due to delay in diagnosis of Tuberculosis due to atypical presentation in HIV patients.
- Another reason is the impaired absorption of Isoniazid & Rifampicin from the gut. Acquired MDR-TB is common in these patients.

- Primary Drug Resistance is also common in HIV TB co-infected patients.
- Persistence of TB bacilli after treatment is high in these patients. So Relapse is common in these patients.
- Nosocomial Drug Resistant TB is also possible in hospitalised HIV patientsas their immunity is low.

Drug Resistant TB in HIV Patients

- MDR-TB among HIV patients in India 2012[1]:
  - Primary MDR-TB: 2.2%
  - Acquired MDR-TB: 11-19%
- MDR-TB suspects are subjected to line probe assayunder criteria C. According to criteria C , all HIV TB patients are MDR TB suspects.
  - Management Plan:
    - MDR TB: Category IV
    - XDR TB: Category V

Pill burden in these patients is very high. In addition to the disease, toxicity of the drugs causes increased morbidity in these patients.

MDR-TB: Definition & Treatment

- A TB patient whose sputum is culture positive for Mycobacterium tuberculosis and is resistant in-vitro to Isoniazid and Rifampicin

with or without other anti-tubercular drugs based on DST results from an RNTCP-certified Culture & DST Laboratory[4]

- Intensive Phase is for 6-9 months. 6 drugs used in this phase are Kanamycin, Pyrazinamide, Ethambutol ,Levofloxacin, Ethionamide and Cycloserine
- The Continuation Phase is for 18 month. The 4 drugs used in this phase are Levofloxacin, Ethambutol, Ethionamide and Cycloserine

XDR-TB: Definition & Treatment

- An MDR TB case whose recovered M. tuberculosis isolate is resistant to at least Isoniazid, Rifampicin, a fluoroquinolone (Ofloxacin, Levofloxacin, or Moxifloxacin) and a second-line injectable anti-TB drug (Kanamycin, Amikacin, or Capreomycin) at a RNTCP-certified Culture & DST Laboratory[4]
- The duration of Intensive Phase is 6-12 months. The 7 drugs used in this phase are Capreomycin, PAS, Clofazimine, Moxifloxacin, High dose-INH, Linezolid, and Amoxyclav
- The duration of Continuation Phase is 18 months. The drugs used in this phase are PAS, Moxifloxacin, Linezolid, High dose-INH, Clofazimine, and Amoxyclav

Isoniazid Prophylaxis Therapy (IPT)[18]

It consists of using isoniazid alone to reduce the incidence of TB in HIV patients. It can be given as daily regimen of 300mg for 6 months. Various studies have been done to assess the efficacy of IPT. The efficacy was just around 36% in most studies. The major challenge in implementing IPT is ruling out active TB infection.

Unless active TB is ruled out, IPT may lead to isoniazid monoresistance. Further studies are needed before implementing IPT in national programme. Rifampicin can also be used for TB prophylaxis.

AIM & OBJECTIVES

AIM:

To determine the correlation between clinical, radiological, microbiological features and the drug resistance pattern of Mycobacterium tuberculosis in patients with HIV tuberculosis co infection.

OBJECTIVES:

1. To determine the relationship between clinical presentation of HIV -pulmonary tuberculosis co infection and drug resistance pattern.
2. Correlate CD4 count and drug resistance pattern.
3. Compare HIV staging and drug resistance pattern.
4. Compare roentgenographic features of HIV TB co-infection patients with sputum DST pattern.
5. Compare sputum for AFB smear status with drug resistance pattern.
6. Compare LPA and Gold standard Sputum culture and sensitivity.
7. Prevalence of MDR TB in HIV tuberculosis co infection.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design : Prospective

Study period : April 2013 to March 2014

Study population : Patients admitted in GHTM

Inclusion Criteria:

1) All HIV seropositive patients with pulmonary TB.

2) Age > 18 years

Exclusion Criteria:

1) HIV patients with only extrapulmonary TB

2) Age < 18 years

3) Patients who are moribund, sick and unable to produce sputum.

4) Patients who are not willing to participate in the study

5)Patients whose sputum showed no growth in LJ culture medium.

METHODS:

Collection of clinical samples/ data:

1. Symptoms duration.

2. HIV diagnosis and treatment history

3. Antituberculous treatment history.

4. Height & Weight.

5. Chest radiograph.

6. Sputum for AFB staining, LPA, sputum Mtb culture

7. CD4 count

8. Allotting score for each of the variable. Predict MDR based on score. Comparing prediction with sensitivity results and analyse.

Features/score	0	1	2
Contact H/o PT	absent		present
H/O ATT	No		Yes
HIV STAGE 4	No	Yes	
CD4 count	>200	<200	
BMI	>18	<18	
Pulmonary TB	alone	with dissemination	
chest xray	no cavity	cavitation	
sputum smear	negative	positive	

Drug susceptibility of all the samples were detected using line probe assay. For those cases which were reported as smear negative by line probe assay, were subjected to Lowenstein Jenson culture. M.Tuberculosis colonies grown in this culture medium were then subjected to line probe assay and drug sensitivity pattern was obtained. All sputum samples were grown in LJ medium and those cases whose culture was positive for M.Tuberculosis alone were included in this study.

Sensitivity pattern obtained by line probe assay were :

LINE PROBE ASSAY REPORT	DIAGNOSIS
Sensitive to isoniazid(H) and rifampicin(R)	Drug susceptible TB
Sensitive to R , Resistant to H	Monoresistant to H
Sensitive to H , Resistant to R	Monoresistant to R
Resistant to H & R	MDR

In this study, Rifampicin monoresistance and MDR are considered together as *Rifampicin resistance.*

Drug resistance includes isoniazid monoresistance, Rifampicin monoresistance and MDR.

Source of the study population:

Government Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai.

Statistical analysis:

Analysis is done using Epi info software.

Ethical Clearance

The various investigations and procedures that will be used in this study will be as per protocol. The identity of each patient will be kept

confidential. This study will not violate medical ethics in anyway and it will help to know the correlation between clinical, radiological, microbiological features and the drug resistance pattern of Mycobacterium tuberculosis in sputum in patients with HIV tuberculosis co infection

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

In the study of correlation of clinical, radiological, microbiological features and drug resistance pattern of mycobacterium tuberculosis in patients with HIV tuberculosis co-infectionthe following observations were made.

In the period April 2013 to March 2014, totally 230 patients were diagnosed to be coinfected with Human Immunodeficiency Virus and Tuberculosis.

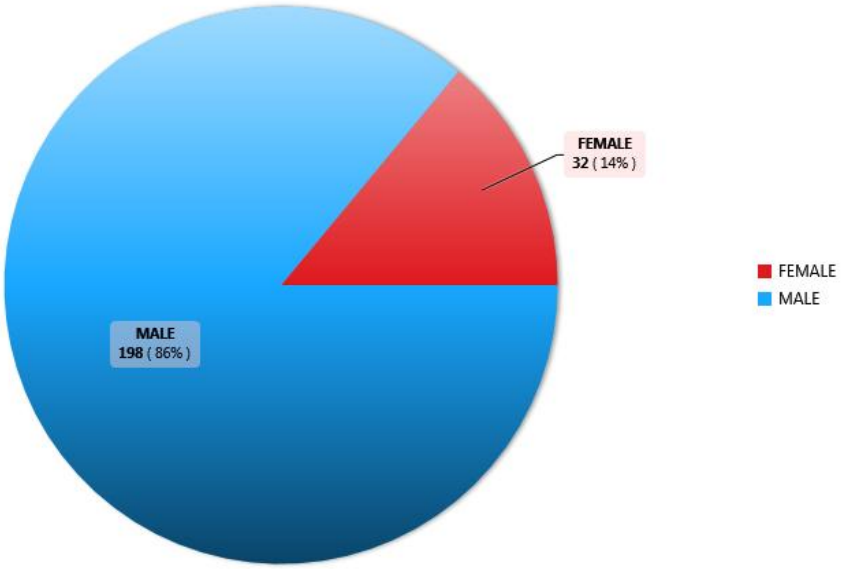
Of these 230 patients, 198 were male, 32 were female. (Table 1)

Sex	**Frequency**	**Percent**	**Cum.Percent**
Male	198	86.09%	86.09%
Female	32	13.91%	100.00%
Total	**230**	**100.00%**	**100.00%**

Table 1

Table 2				
	Obs	**Mean**	**Std Dev**	**Range**
AGE	230	39.54	8.49	18-65

Mean age of the patients is 39.5(Table 2)



Sex distribution

Prevalence of MDR TB

Rifampicin monoresistance and MDR are considered together as *Rifampicin resistance*. *Drug resistance* includes isoniazid monoresistance, Rifampicin monoresistance and MDR.

Total number of HIV TB co-infected cases is 230. 12 cases were found to be MDR TB,14 cases were monoresistant to isoniazid and 11 cases were monoresistant to rifampicin(Table 3)

Table 3

Sensitivity pattern	Frequency	Percent	95% CI Lower	95% CI Upper
Sensitive to H,R	193	83.9%	78.51%	88.41%
Monoresistant To H	14	6.1%	3.37%	10.00%
Monoresistant To R	11	4.8%	2.41%	8.40%
MDR	12	5.2%	2.72%	8.94%
Total	230	100%		

Prevalence of MDR TB in HIV TB co infected patients is 5.2 %. Prevalence of Rifampicin Resistant TB cases is 10%.

Table 4

TB CASE	Frequency	Percent	95% CI Lower	95% CI Upper
New	148	64%	57.79%	70.53%
Retreatment	82	36%	29.47%	42.21%
TOTAL	230	100.00%		

Out of 230 cases, 148(64%) were new TB cases and 82(36%) were retreatment cases (Table 4).Their drug sensitivity pattern is as follows :

Prevalence of MDR in new cases is 3.4%. It rises to 8.5 % in retreatment cases.(Table 5& 6)

Prevalence of Rifampicin resistanceis 6.1%in new cases and 19% in retreatment cases.(Table 5& 6)

NEW TB CASE

Table 5

Sensitivity Pattern	Frequency	%	95%CI Lower	95% CI Upper
Sensitive to H ,R	132	89.2%	83.04%	93.69%
Monoresistant to H	7	4.7%	1.92%	9.50%
Monoresistant to R	4	2.7%	0.74%	6.78%
MDR	5	3.4%	1.11%	7.71%
Total	148	100%		

RETREATMENT TB CASE

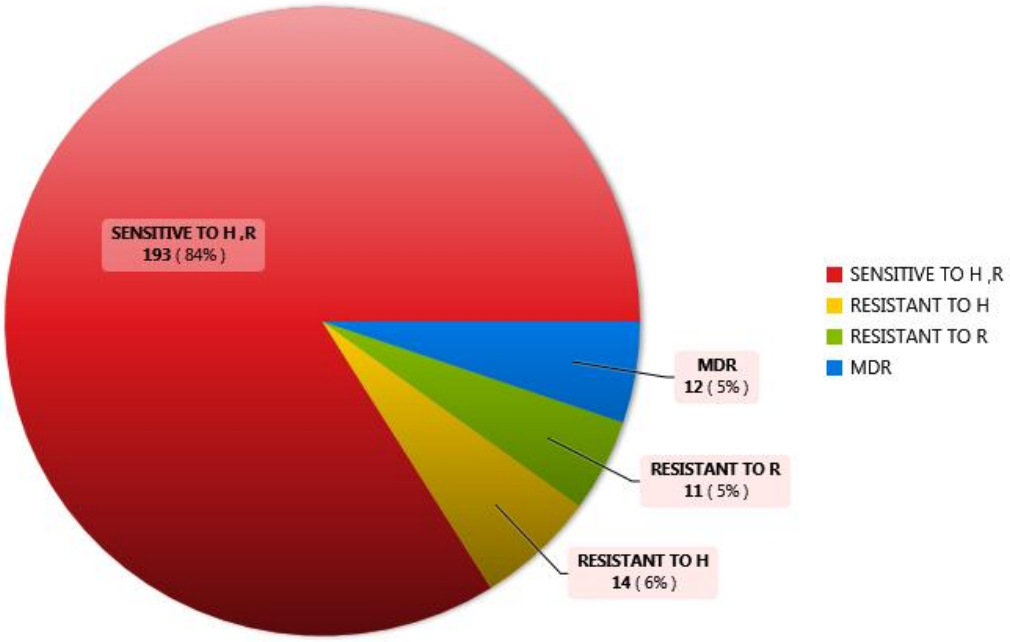
Table 6

Sensitivity Pattern	Frequency	%	95% CI Lower	95% CI Upper
Sensitive to H ,R	61	74.4 %	63.56%	83.40%
Monoresistant to H	7	8.5%	3.50%	16.80%
Monoresistant to R	7	8.5%	3.50%	16.80%
MDR	7	8.5%	3.50%	16.80%
TOTAL	82	100%		

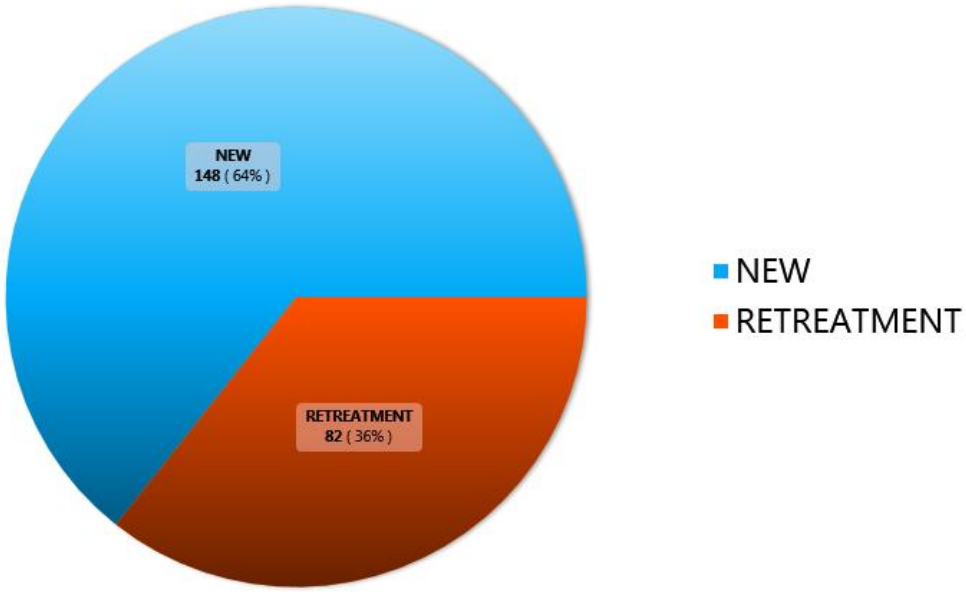
In newly detected TB cases , 89.2% are dug susceptible TB, 4.7% are isoniazid monoresistant , 2.7% are rifampicin monoresistant and 3.4% are MDR cases.(Table 5)

In retreatment TB cases , 74.4% are dug susceptible TB, 8.5% are isoniazid monoresistant , 8.5% are rifampicin monoresistant and 8.5% are MDR cases.(Table 6)

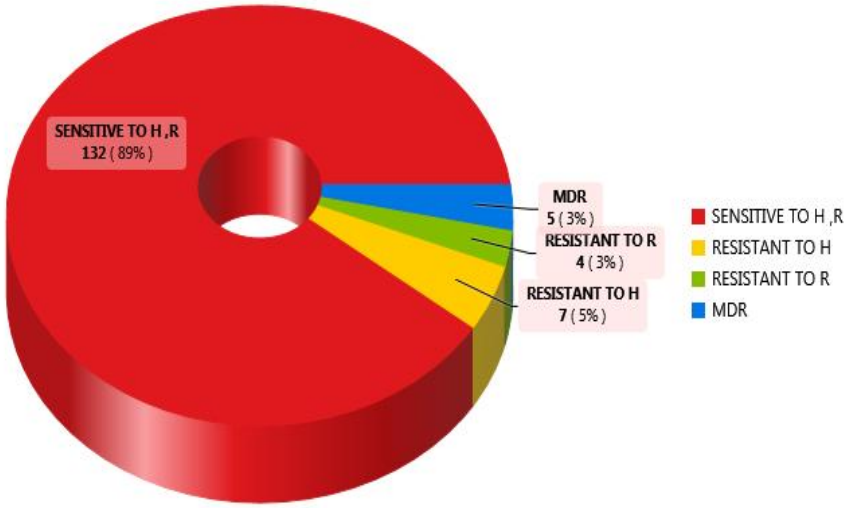
DRUG RESISTANCE PATTERN



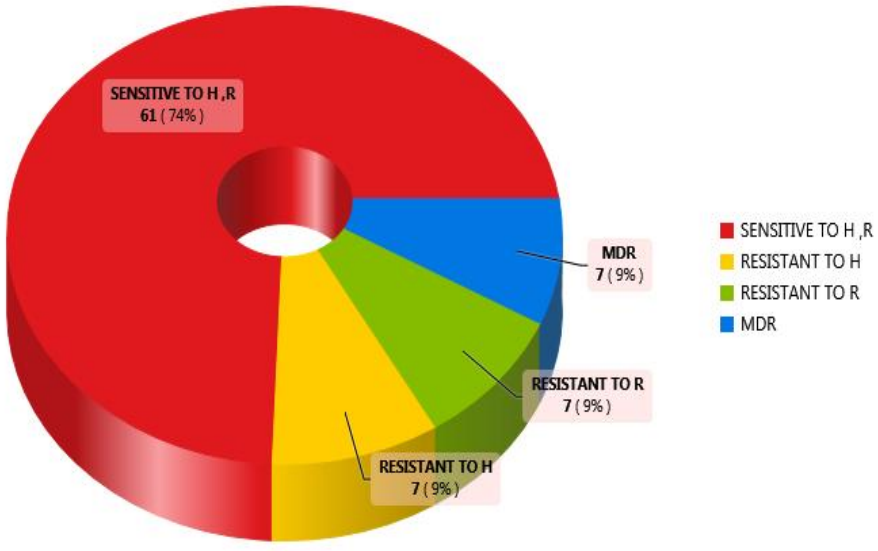
TUBERCULOSIS CASE



New cases and drug resistance pattern



Retreatment Cases & drug resistance pattern



Correlation between clinical presentation and drug resistance pattern

Clinical variables like TB Case (new or retreatment), HIV treatment(ART / not on ART),disseminated TB and duration of symptoms are compared with drug resistance pattern.

TB case and drug resistance pattern

Drug resistance which includes resistance to single or both drugs is compared with tuberculosis case whether new or retreatment case.Odds ratio is 2.84 (1.39-5.82). p value is 0.003($p<0.05$). p value is significant. (Table 7)

Table 7

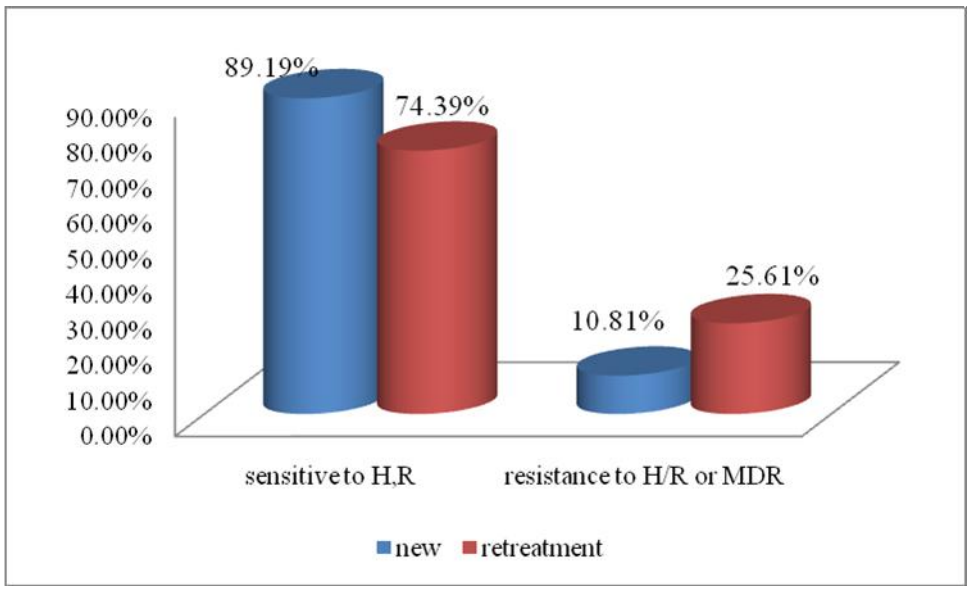
	Sensitivity pattern		
TB Case	Resistant to H/R/H&R	Sensitive to H& R	Total
Retreatment	21	61	82
New	16	132	148
Total	37	193	230
Odds Ratio	2.84	95% CI(1.39 - 5.82)	
Chi-square –p value	0.003		

Rifampicin resistance is compared with TB case. Odds ratio is 3.18 (95%Cl 1.31-7.71). p value is 0.008(<0.05). p value is significant. (Table 8)

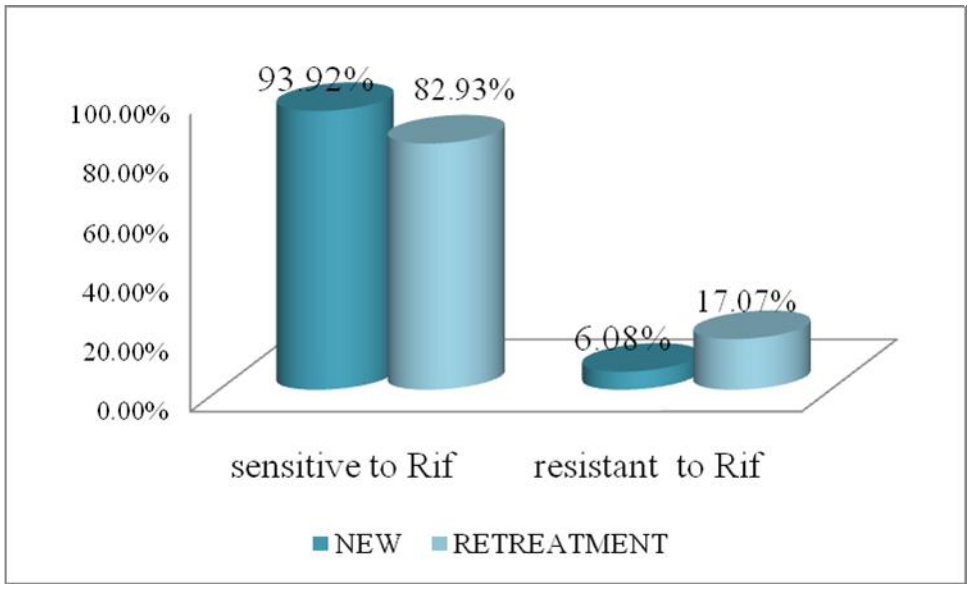
Table 8

TB CASE	Sensitive to R	Resistant to R	Total
NEW	139	9	148
RETREATMENT	68	14	82
Total	207	23	230
Odds Ratio	3.18(95%CI 1.31- 7.71)		
Chi-square –p value	0.008		

Drug resistance and TB case



Rifampicin resistance and TB case



HIV treatment and drug resistance pattern

Drug resistance of patients who were on ART was compared with those who were not on ART. 94 patients were on ART and 136 were not on ART. (Table 9)

Table 9

	patients on ART		not on ART	
Sensitivity	**Frequency**	**Percent**	**Frequency**	**Percent**
sensitive to R	82	87%	125	92%
Resistant to R	12	13%	11	8%
TOTAL	**94**	**100.00%**	**136**	**100.00%**

Table 10

ON ART		
TB CASE = NEW		
Sensitivity	**Frequency**	**%**
sensitive to R	30	100%
resistant to R	0	0%
TOTAL	**30**	**100%**
TB CASE = RETREATMENT		
Sensitivity	**Frequency**	**%**
sensitive to R	52	81%
resistant to R	12	19%
TOTAL	**64**	**100.%**

Rifampicin resistance is seen in 13% of cases who are on ART and in 8% of ART naïve cases. (Table 9)

Table 11

NOT ON ART		
TB CASE = NEW		
Sensitivity	**Frequency**	**%**
sensitive to R	109	92%
resistant to R	9	8%
TOTAL	**118**	**100%**
TB CASE = RETREATMENT		
Sensitivity	**Frequency**	**%**
sensitive to R	16	89%
resistant to R	2	11%
TOTAL	**18**	**100%**

In patient on ART group there is no case of Rifampicin resistance in newly detected TB cases while in other group, there is 8% of rifampicin resistance in newly detected TB cases.(Table 10 &11)

HIV treatment and Rifampicin resistance is compared. Odds ratio is 0.60 (95%CI 0.25 – 1.43). p value is 0.24 (>0.05). p value is not significant. (Table 12)

Table 12

	Sensitivity pattern		
HIV treatment	Sensitive to R	Resistant to R(including MDR)	Total
on ART	82	12	94
not on ART	125	11	136
Total	207	23	230
Odds Ratio	0.60(95% CI 0.25 -1.43)		
Chi-square - p value	0.24		

Disseminated TB and drug resistance pattern

Drug resistance pattern in pulmonary TB with and without dissemination. 10% of disseminated TB cases are MDR TB. 20 % are Rifampicin resistant. (Table 13)

Table 13

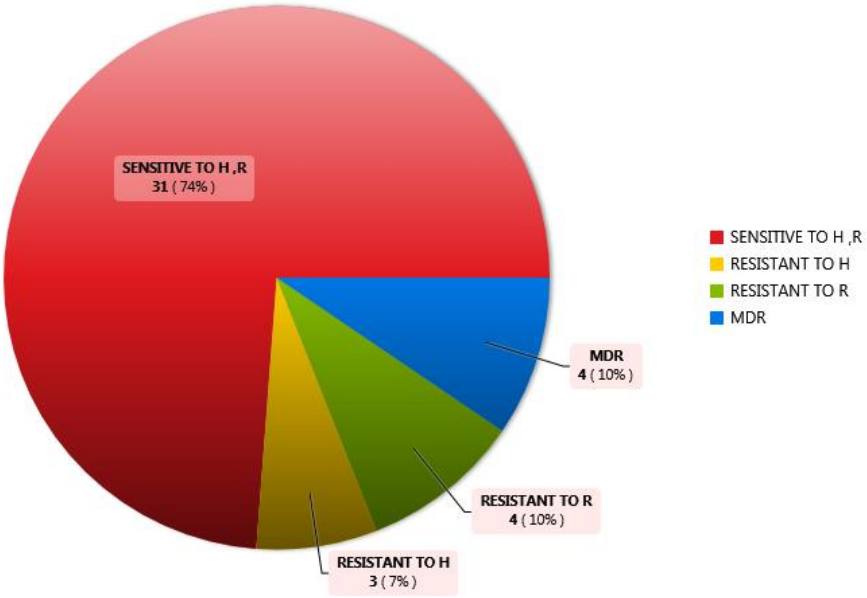
Pulmonary TB with dissemination		
Sensitivity pattern	**Frequency**	**Percent**
Sensitive to H ,R	31	74%
Monoresistant to H	3	7%
Monoresistant to R	4	10%
MDR	4	10%
TOTAL	**42**	**100%**

Table 14

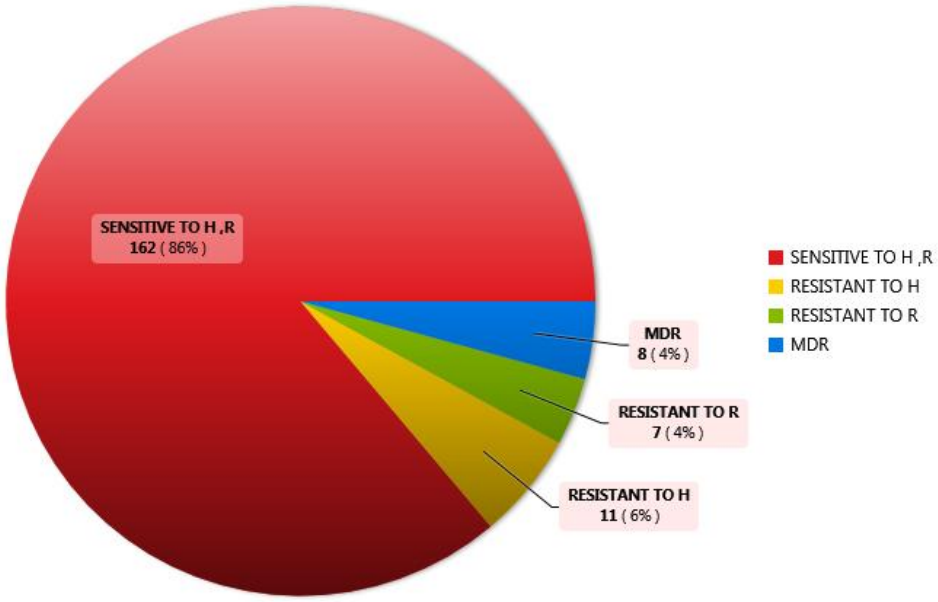
Pulmonary TB without dissemination		
Sensitivity pattern	**Frequency**	**Percent**
Sensitive to H ,R	162	86%
Monoresistant to H	11	6%
Monoresistant to R	7	4%
MDR	8	4%
TOTAL	**188**	**100%**

MDR TB constitutes just 4% in TB without dissemination. (Table 14)

Drug resistance pattern in disseminated TB



Drug resistance pattern in TB without dissemination



The association between disseminated TB and drug resistance pattern is assessed. Odds ratio is 2.21 (95%Cl 1.0-4.9). p value is 0.048.(<0.05). p value is significant. (Table 15)

Table 15

	Sensitivity pattern		
Disseminated TB	Sensitive to H,R	Resistant to H/R/H&R	Total
No	162	26	188
Yes	31	11	42
Total	193	37	230

The association between disseminated TB and rifampicin resistance pattern is assessed. Odds ratio is 2.71(95%CL 1.07-6.09). p value is 0.03(<0.05).p value is significant. (Table 16)

Table 16

	Sensitivity pattern		
Disseminated TB	Sensitive to R	Resistant to R (including MDR)	Total
No	173	15	188
Yes	34	8	42
Total	207	23	230

Comparison of duration of symptoms and drug resistance pattern

4% of cases had MDR TB when duration of symptoms was less than 3 months. (Table 17) 12.9% cases had MDR TB when duration of symptoms was more than 3 months. (Table 18)

Table 17

Symptoms duration <3months			
Sensitivity pattern	Frequency	Percent	95% CI
Sensitive to H, R	167	84%	78% -88%
Monoresistant to H	13	7%	3%– 11%
Monoresistant to R	11	5%	3% - 10%
MDR	8	4%	2%– 8%
TOTAL	199	100.00%	

Table 18

symptoms duration >3months			
Sensitivity Pattern	Frequency	Percent	95% CI range
Sensitive to H ,R	26	84%	66 % - 94 %
Monoresistant to H	1	3%	0% - 17%
Monoresistant to R	0	0%	0% - 11%
MDR	4	13%	4% - 30%
Total	31	100.00%	

The association between duration of symptoms and drug resistance pattern is assessed. Odds ratio is1.0.P value is 0.99.p value is not significant. (Table 19)

Table 19

	Sensitivity pattern		
duration of symptoms	Sensitive to H, R	Resistance to H,R or H&R	Total
<3months	167	32	199
>3months	26	5	31
Total	193	37	230
Odds Ratio	1.00 (95% CI 0.36 - 2.81)		
Chi-square–p value	0.99		

The association between duration of symptoms and rifampicin resistance pattern is assessed. Odds ratio is 1.4. p value is 0.56 (>0.05) p value is not significant. (Table 20)

Table 20

symptoms duration	Sensitivity pattern		Total
	sensitive to R	Resistant to R (including MDR)	
<3months	180	19	199
>3months	27	4	31
Total	207	23	230

	Point	95% Confidence Interval	
	Estimate	Lower	Upper
Odds Ratio	1.40	0.44	4.44

	P value
Chi-square	0.56

Comparison of CD4 count and drug resistance pattern

When the CD4 count was less than 200, MDR TB was present in 8% of cases. In patients whose CD4 count is more than 200, MDR TB was seen in 1% of cases. (Table 21 &22)

Table 21

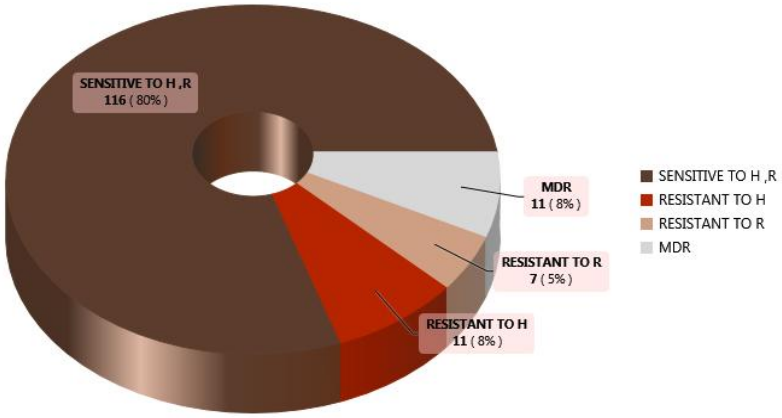
CD4 COUNT <200				
Sensitivity pattern	**Frequency**	**Percent**	**95% CI Lower**	**95% CI Upper**
Sensitive to H ,R	116	80%	73%	86%
Monoresistant to H	11	8%	4%	13%
Monoresistant to R	7	5%	2%	10%
MDR	11	8%	4%	13%
Total	**145**	**100.00%**		

Table 22

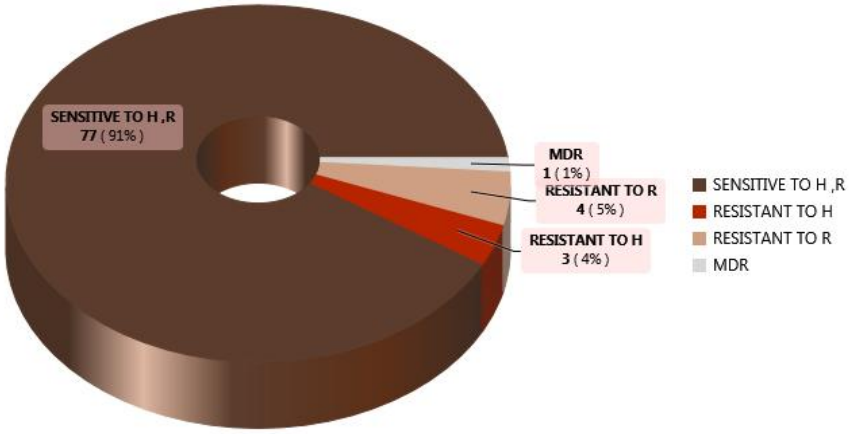
CD4 COUNT >200				
Sensitivity pattern	**Frequency**	**Percent**	**95% CI Lower**	**95% CI Upper**
Sensitive to H ,R	77	91%	82%	96%
Monoresistant to H	3	4%	1%	10%
Monoresistant to R	4	5%	1%	12%
MDR	1	1%	0%	6%
Total	**85**	**100.00%**		

Drug susceptible TB is present in 80% of cases when CD4 count is less than 200. It rises to 91% cases when the CD4 count is more than 200.

CD4 count less than 200 and drug resistance pattern



CD4 count more than 200 and drug resistance pattern



CD4 count is compared with drug resistance pattern. Odds ratio is 2.41(95%Cl 1.05 -5.54). p value is 0.035 (<0.05). p value is significant. (Table 23)

Table 23

	Sensitivity pattern		
CD4 COUNT	Resistance to H,R or H&R	Sensitive to H, R	Total
<200	29	116	145
>200	8	77	85
Total	37	193	230

	Point	95% Confidence Interval	
	Estimate	Lower	Upper
Odds Ratio	2.41	1.05	5.54
Chi-square – p value	0.035		

Table 24

	Sensitivity pattern		
CD4 COUNT	MDR	Sensitive to H,R	Total
<200	11	116	127
>200	1	77	78
Total	12	193	205
	Estimate	Lower	Upper
Odds Ratio	7.30	0.92	57.71
Chi-square - p value	0.029		

CD4 count is compared in patients with MDR TB and sensitive cases. Odds ratio is 7.30(95%Cl 0.92-57.71). p value is 0.029(<0.05). p value is significant. (Table 24)

Comparison of HIV staging and drug resistance pattern

Rifampicin resistance is seen in 17% of HIV stage 4 cases. It is seen in 7% of HIV stage 3 cases. (Table 25, 26)

Table 25

HIV STAGE 4			
Sensitivity pattern	Frequency	Percent	95% CI
sensitive to R	54	83%	72%-91%
Resistant to R (including MDR)	11	17%	9%-28%
TOTAL	65	100%	

Table 26

HIV STAGE 3			
Sensitivity pattern	Frequency	Percent	95% CI
sensitive to R	153	93%	88%-96%
Resistant to R (including MDR)	12	7%	4%-12%
TOTAL	165	100%	

HIV stage is compared with drug resistance pattern. Odds ratio is 1.95. p value is 0.07(>0.05)p value is not significant. (Table 27)

Table 27

	Sensitivity pattern		
HIV STAGE	Resistance to H,R or H&R	Sensitive to H, R	Total
Stage 4	15	50	65
Stage 3	22	143	165
Total	37	193	230
	Estimate	Lower	Upper
Odds Ratio	1.95	0.94	4.05
Chi-square - p value	0.070		

Table 28

	Sensitivity pattern		
HIV Stage	Resistant to R (including MDR)	Sensitive to R	Total
Stage 4	11	54	65
Stage 3	12	153	165
Total	23	207	230
	Estimate	Lower	Upper
Odds Ratio	2.59	1.08	6.23
Chi-square - p value	0.028		

HIV stage is compared with rifampicin resistance. Odds ratio is 2.59. p value 0.028(<0.05).p value is significant. (Table 28)

Roentgenographic features and drug resistance pattern

Lung fields in chest x-ray are usually divided into 3 zones. Upper zone extends from apex to second costal cartilage. Mid zone extends from second to fourth costal cartilage. Lower zone extends from 4th costal cartilage to diaphragm. Thus lung fields are divided into 6 zones, 3 on each side.. Number of zones in chest x-ray is compared with drug resistance pattern. Odds ratio is 2.30. p value is 0.094 (>0.05). p value is not significant. (Table 29)

Table 29

	Sensitivity pattern		
ZONES	Sensitive to H, R	Resistance to H,R or H&R	Total
>3	51	5	56
<3	142	32	174
Total	193	37	230
	Estimate	Lower	Upper
Odds Ratio	2.30	0.85	6.22
Chi-square - p value	0.094		

Table 30

	Sensitivity pattern		
Zones	Sensitive to R	Resistant to R (including MDR)	Total
>3	52	4	56
<3	155	19	174
Total	207	23	230
Odds Ratio	1.60 (95% CI 0.52-4.90)		
Chi-square - p value	0.41		

Number of zones in chest xray is compared with drug resistance pattern. Odds ratio is 1.60. p value is 0.41.p value is not significant. (Table 30)

Cavitation is compared with drug resistance pattern. (Table 31)

Table 31

	cavity present		without cavity	
Sensitivity pattern	Frequency	%	Frequency	%
Sensitive to H ,R	21	81%	172	84%
Monoresistant to H	1	4%	13	6%
Monoresistant to R	3	12%	8	4%
MDR	1	4%	11	5%
TOTAL	26	100%	204	100 %

When presence of cavity is compared with drug resistance pattern the odds ratio is 0.78. p value is 0.22.p value is not significant. (Table 32)

Table 32

	Sensitivity pattern		
CAVITATION	Sensitive to H, R	Resistance to H,R or H&R	Total
Yes	21	5	26
No	172	32	204
Total	193	37	230
Odds Ratio	0.78 (95%CI 0.28-2.22)		
Chi-square - p value	0.22		

Comparison of sputum smear for AFB and drug resistance pattern

Out of 230 cases , 148 (64%)cases were sputum positive for AFB and 82 (36%)cases were smear negative for AFB. (Table 33)

Table 33

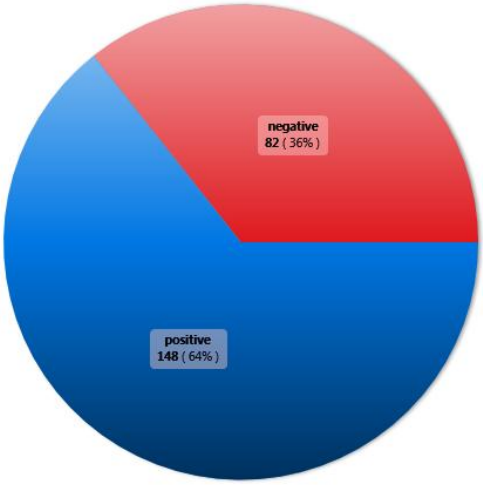
Sputum smear	Frequency	Percent
Negative	82	35.65%
Positive	148	64.35%
Total	230	100.00%

Table 34

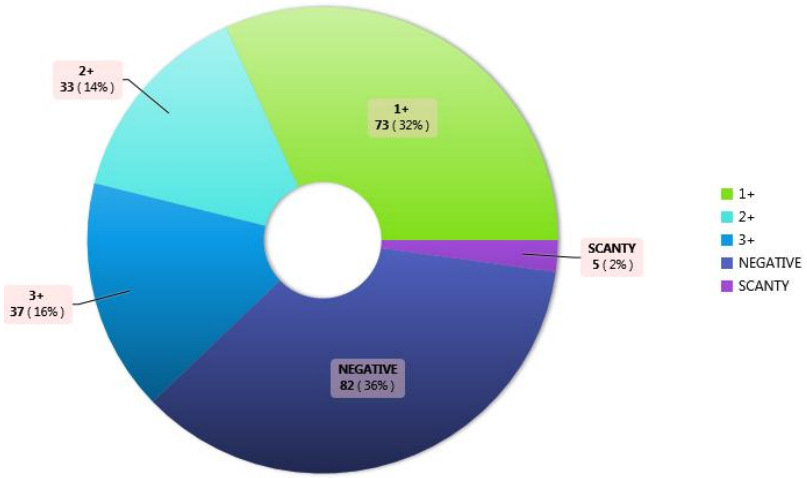
Sputum smear	**Frequency**	**Percent**
Negative	82	36%
Scanty	5	2%
1+	73	32%
2+	33	14%
3+	37	16%
TOTAL	**230**	**100.00%**

Out of the 64% sputum smear positive cases, 16 % had smear grading 3+, 14% with grading of 2+ , 32% with grading 1+ and 2% had scanty bacilli. (Table 34)

Sputum smear status



Sputum smear frequency



Drug resistance pattern in sputum smear positive and sputum smear negative cases is shown below. (Table 35, 36)

Table 35

Sputum smear negative cases		
Sensitivity pattern	Frequency	Percent
Sensitive to H ,R	66	80%
Monoresistant to H	7	9%
Monoresistant to R	6	7%
MDR	3	4%
Total	82	100.00%

Table 36

Sputum smear positive cases		
Sensitivity pattern	Frequency	Percent
Sensitive to H ,R	127	86%
Monoresistant to H	7	5%
Monoresistant to R	5	3%
MDR	9	6%
TOTAL	148	100.00%

Prevalence of MDR in sputum smear negative cases is 4% and in sputum smear positive cases, it is 6%. (Table 35, 36)

Sputum smear for acid fast bacilli is compared with drug resistance pattern. Odds ratio is 1.47. p value is 0.29(>0.05).p value is not significant. (Table 37)

Table 37

	Sensitivity		
Sputum smear	Sensitive to H, R	Resistance to H,R &H&R	Total
Positive	127	21	148
Negative	66	16	82
Total	193	37	230
	Estimate	Lower	Upper
Odds Ratio	1.47	0.72	3.0
Chi-square - p value	0.29		

Sputum smear for acid fast bacilli is compared with rifampicin resistance (including MDR TB cases). (Table 38)

Table 38

	Sensitivity pattern		
Sputum smear	Sensitive to R	Resistant to R (including MDR)	Total
Positive	134	14	148
Negative	73	9	82
Total	207	23	230

Odds ratio is 1.18 (95% CI 0.49 – 2.86). p value is 0.71 (>0.05).p value is not significant. (Table 38)

Comparison of Line probe assay and Lowenstein Jenson culture

Line probe assay results which showed smear negative was compared with culture and drug sensitivity. Out of 230 cases, drug sensitivity pattern was obtained directly using line probe assay in 154 cases. (Table 39)76 cases were smear negative by line probe assay. (Table 40)

Table 39

Line probe assay		
Sensitivity pattern	Frequency	Percent
Sensitive to H ,R	130	84%
Monoresistant to H	9	6%
Monoresistant to R	7	5%
MDR	8	5%
Total	154	100.00%

Those 76 cases were subjected to culture and drug sensitivity pattern obtained by subjecting culture isolates to line probe assay. (Table 40)

Table 40

Culture LJ medium		
Sensitivity pattern	Frequency	Percent
Sensitive to H ,R	63	83%
Monoresistant to H	5	7%
Monoresistant to R	4	5%
MDR	4	5%
TOTAL	76	100.00%

Table 41

Sensitivity pattern = Sensitive to H ,R		
LPA	**Frequency**	**Percent**
Smear negative	63	33%
Sensitive To H & R	130	67%
TOTAL	193	100.00%

Table 42

Sensitivity pattern = Monoresistant to H		
LPA	**Frequency**	**Percent**
Smear negative	5	36%
Monoresistantto H	9	64%
TOTAL	14	100.00%

Table 43

Sensitivity pattern = Monoresistant to R		
LPA	**Frequency**	**Percent**
Smear negative	4	36%
Resistant To R Alone	7	64%
TOTAL	11	100.00%

Table 44

Sensitivity pattern = MDR		
LPA	**Frequency**	**Percent**
Smear negative	4	33%
MDR	8	67%
TOTAL	12	100.00%

This table shows that 67% of MDR TB cases were detected using line probe assay and only 33% required Lowenstein Jenson culture to identify the drug sensitivity pattern. (Table 44)

Scoring and drug resistance

Table 45

Features/score	0	1	2
Contact H/o PT	absent		present
H/O ATT	No		Yes
HIV STAGE 4	No	Yes	
CD4 count	>200	<200	
BMI	>18	<18	
Pulmonary TB	alone	with dissemination	
chest xray	no cavity	cavitation	
sputum smear	negative	positive	

Scoring was done using these variables (Table 45). Maximum score possible was 10. Patients were divided into two groups with a cutoff point of 4. (Table 46, 47)

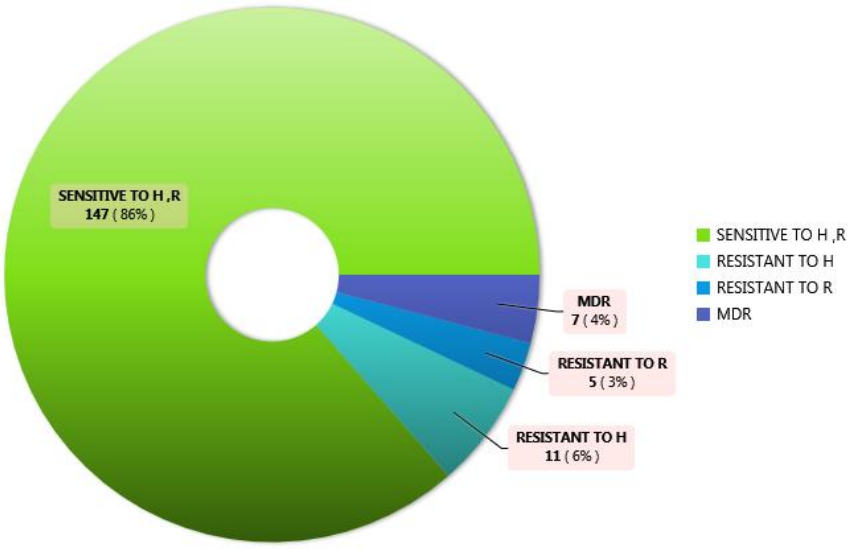
Table 46

Score less than 4		
Sensitivity pattern	**Frequency**	**Percent**
Sensitive to H ,R	147	86%
Monoresistant to H	11	6%
Monoresistant to R	5	3%
MDR	7	4%
Total	**170**	**100.00%**

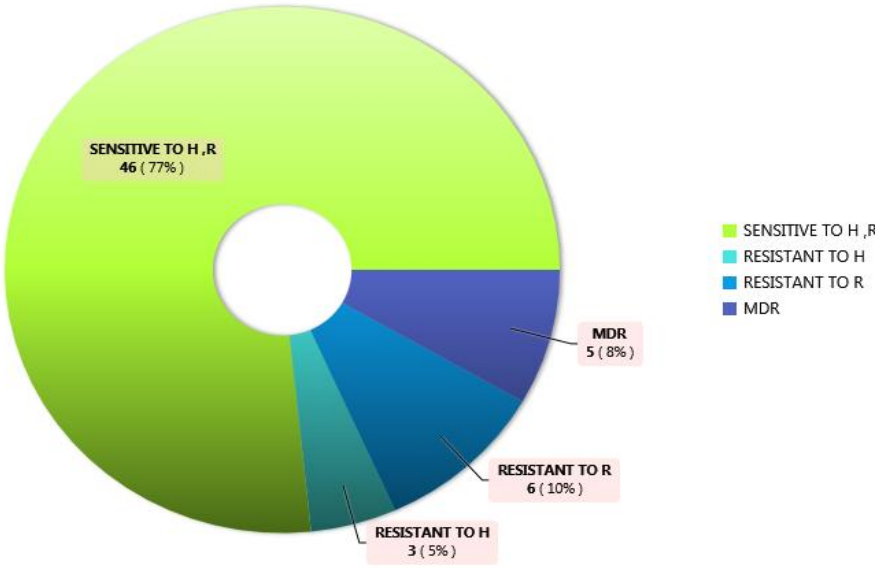
Table 47

Score more than 4		
Sensitivity pattern	**Frequency**	**Percent**
Sensitive to H,R	46	77%
Monoresistant to H	3	5%
Monoresistant to R	6	10%
MDR	5	8%
Total	**60**	**100.00%**

Score less than 4 and drug resistance pattern



Score more than 4 and drug resistance pattern



This shows that drug susceptible cases are 86% when score is less than 4. It falls to 77% when score is more than 4. (Table 46, 47)

Scoring and drug resistance pattern is compared.

Table 48

	Sensitivity pattern		
Score	Sensitive to H, R	Resistance to H,R orH&R	Total
Less than 4	147	23	170
More than 4	46	14	60
Total	193	37	230

Odds ratio is 1.95 (95%Cl 0.93 - 4.09). Chi square gives p value of 0.076(>0.05). p value is not significant. (Table 48)

Scoring and Rifampicin resistance

Comparison of score and rifampicin resistance is shown in following table. (Table 49)

Table 49

	Sensitivity pattern		
Score	Sensitive to R	Resistant to R (including MDR)	Total
Less than 4	158	12	170
More than 4	49	11	60
Total	207	23	230

Odds ratio is 2.96 (95% Cl 1.23 – 7.12). p value is 0.01(<0.05).p value is significant. (Table 49)

DISCUSSION

DISCUSSION

In the following discussion, Rifampicin monoresistance and MDR are considered together as Rifampicin resistance. Drug resistance includes isoniazid monoresistance, Rifampicin monoresistance and MDR.

Prevalence of MDR TB

In India, according to WHO report 2013, the estimated the prevalence of MDR-TB is about 2.2% in new cases and 15% (11-19%) in re-treatment cases[1].

This study shows prevalence of MDR TB to be 3.4% in new cases and 8.5% in retreatment cases. Prevalence of Rifampicin resistance in new cases is 6.1% and that in retreatment cases is 19%. It was also found that prevalence of drug sensitive TB fell from 89% in new cases to 74% in retreatment cases.

Clinical presentation

Clinical variables like type of TB case (New or retreatment), treatment for HIV, disseminated TB and duration of symptoms were compared with drug resistance pattern.

Tuberculosis case

When type of TB case (new or retreatment) was compared with drug resistance pattern, it was found that drug resistance was 2.8 times more common in retreatment case. Odds ratio was 2.84 (95% CI 1.39–5.82). P value obtained by chi square was 0.003(<0.05). p value is significant. There is strong correlation between retreatment and drug resistance. It was shown that Rifampicin resistance was 3.2 times more likely in retreatment cases. *There was significant association between retreatment case and Rifampicin resistance [p value 0.008 (<0.05)]*

It is similar to the results obtained from the study of Rajasekaran et al, which showed prevalence of drug resistance is more in chronic TB patients[34].

HIV treatment

Drug resistance pattern of patients who were on ART was compared with those who are not on ART. 94 (41%)patients were on ART while 136(59%) were ART naïve.

Rifampicin resistance in patients taking ART was 13% compared to 8% in other group.It may appear controversial as patients on ART have more Rifampicin resistance. But on analyzing the prior history of treatment for tuberculosis, it shows that there was no case of Rifampicin resistance in newly detected TB cases, when the patient is on ART. Rifampicin resistance was present in 8% of newly detected TB cases when patient is not on ART. But Rifampicin resistance was more(12 cases) in retreatment cases of TB in patients taking ART, compared to 2 cases in retreatment of tuberculosis in patients not on ART.

HIV treatment is not associated with Rifampicin resistance. This is shown by odds ratio of 0.60 and p value 0f 0.24. p value is not significant.

Disseminated TB

Drug resistance pattern in pulmonary TB with dissemination was compared with pulmonary TB without dissemination. Rifampicin resistance was 20 % in disseminated TB group compared to 8 % in pulmonary TB without dissemination. Drug susceptible TB constituted 74 % in disseminated TB group, compared to 86% in pulmonary TB without dissemination. Drug resistance was 2.2 times more likely in disseminated TB group [Odds ratio was 2.2(95% CI 1.0 - 4.9)]. Rifampicin resistance was 2.7 times more likely in disseminated TB group [Odds ratio 2.7(95%CI 1.07- 6.09). *Association between Rifampicin resistance and disseminated TB is statistically significant*. P value is 0.03(<0.05).

Duration of symptoms

Rifampicin resistance was 9% when symptoms' duration was less than 3 months and 13% when duration was more than 3 months. Drug susceptible TB was 84% in both groups. There was no significant association between Rifampicin resistance and duration of symptoms. P value is 0.56 (>0.05). p value is

not significant. *Thus Rifampicin resistance must be suspected in all cases irrespective of duration of symptoms.*

CD4 count

When the CD4 count is less than 200, MDR TB was seen in 8% of cases. But with higher CD4 count, MDR TB constitutes just 1% of cases. Rifampicin resistance was 13% in group with low CD4 count compared to 6% in other group. Drug resistance was 2.4 times more likely when CD4 count is low.[Odds ratio 2.41(95% CI 1.05 – 5.54)]. *MDR TB was 7.3 times more likely when CD4 count is less than 200*. [Odds ratio 7.3 (95%CI 0.92 – 57.71)]. There is a strong association between MDR TB and low CD4 count. P value is 0.029 (<0.05). p value is significant.

HIV stage

Pulmonary TB indicates HIV stage 3. Extrapulmonary TB constitutes HIV stage 4. Rifampicin resistance was present in 17% of cases in stage 4 and in 7% cases in stage 3. There

was no significant association between drug resistance and stage of HIV disease. p value is 0.07(>0.05). But *Rifampicin resistance was 2.6 times more likely in HIV stage 4* [Odds ratio 2.6(95%CI 1.08 – 6.23)]. Rifampicin resistance was significantly associated with HIV stage 4. p value 0.028(<0.05). p value is significant.

Chest X-ray features

Presence or absence of 3 or more zones in a chest x-ray was compared with drug resistance pattern. *There was no significant association* between them. p value is 0.094(>0.05). p value is not significant.

Cavitation

Out of total 230 cases, cavity was present only in 26 cases. Out of 12 MDR cases, cavity was present only in one case. *There was no significant association between cavitation and drug resistant TB.* P value is 0.22(>0.05).p value is not significant.

Sputum smear for AFB

148 cases (64%) were sputum smear positive for AFB. Rest 82 cases (36%) were smear negative for AFB. Among these cases 2% had scanty bacilli, 32% had grade 1+, 14% had grade 2+, 16% had grade 3+.

MDR TB among smear negative cases is 4% compared to 6% in smear positive cases. Rifampicin resistance was 11% in smear negative cases and 9 % in smear positive cases. *There was no significant association between sputum smear status and Rifampicin resistance*. p value is 0.71(>0.05). p value is not significant. Thus drug resistance must be suspected irrespective of sputum smear status.

Line probe assay

Sensitivity pattern was directly detected by line probe assay from sputum samples in 154(67%) cases. *Sensitivity of LPA is 67% in this study group*. Rest 76 cases (33%) were smear negative by line probe assay. These 76 samples were

inoculated in LJ culture and colonies grown were subjected to LPA. Rifampicin resistance was 10% in both groups.

Among 12 MDR TB cases, LPA was able to detect 8 cases (67%) directly from sputum sample while 4 cases (33%) were detected after using LJ culture medium. Sensitivity of LPA is 67% in drug susceptible TB, 64 % in isoniazid monoresistant cases and 64 % in Rifampicin monoresistant cases. This is due to paucibacillary state of sputum in HIV positive patients. *This decreased sensitivity of LPA in HIV patients, highlights the need for various rapid diagnostic methods in this high risk group of patients.*

MDR prediction score

This score was sum of variables like contact history of tuberculosis, prior TB treatment history, HIV stage, CD4 count, BMI, disseminated TB, cavitation, sputum smear status. First 2 variables were given values of 0 or 2, other variables

were given value of 0 or 1. Scoring was out of 10 with 0 as minimum value. Cut off point was arbitrarily taken as 4.

Rifampicin resistance was present in 18 % of cases when score was more than 4 and in 7% cases when score was less than 4. *Rifampicin resistance was 3 times more likely when score is more than 4*[Odds ratio 2.96(95%CI 1.23-7.12)] . There is a significant association between Rifampicin resistance and score more than 4. P value is 0.01(<0.05). p value is significant.

In a study by Telzak et al, history of prior treatment for tuberculosis was the only predictor for MDR-TB in a group of HIV-infected patients with tuberculosis.

CONCLUSION

In summary, prevalence of MDR TB in this study is 2.2% in new cases and 8.5% in retreatment cases. Prevalence of Rifampicin resistance in new cases is 6.1% and that in retreatment cases is 19%.

History of prior treatment of tuberculosis, HIV stage 4, disseminated TB were significantly associated with rifampicin resistance.

In this study, *CD4 count less than 200* was significantly associated with MDR TB and drug resistant TB.

HIV treatment was not associated with drug resistance pattern. Duration of symptoms did not affect prevalence of MDR TB. There was no significant association between chest x ray lesions, cavitation with MDR TB. Sputum smear status had no significant relation with MDR TB.

Scoring with 8 variables with score more than 4 was significantly associated with Rifampicin resistance. Since the

study population is small, further studies with large study population will be helpful in validating this score.

Sensitivity of line probe assay in this study is 67%.Since scoring has significant association with Rifampicin resistant TB, it can help in predicting drug resistance in those cases for which are smear negative by LPA. These cases may be subjected to other diagnostic modalities like bronchoscopy , gene expert for early diagnosis of MDR TB. New techniques are required for rapid diagnosis in this paucibacillary state is required. This will help in reducing morbidity and mortality of HIV TB co-infected patients.

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Annexures

PROFORMA

- Name :
- Age :
- Gender :
- Height/Weight :
- Body mass index :
- On ART / Not on ART :
- Contact history of Tuberculosis: Yes/No
- Previous history of Tuberculosis treatment:
- HIV stage 4 :Yes/No
- Disseminated tuberculosis :Yes/No
- Symptoms duration :
- Laboratory investigations : Chest Xray, Sputum Smear for AFB, HIV, CD4 count, ,LPA, DST
- Cavities in chest x-ray :Yes/No
- Zones involved in xray :
- Score :

Scoring done using following variables

Features/score	0	1	2
Contact H/o PT	absent		present
H/O ATT	No		Yes
HIV STAGE 4	No	Yes	
CD4 count	>200	<200	
BMI	>18	<18	
Pulmonary TB	alone	with dissemination	
chest xray	no cavity	cavitation	
sputum smear	negative	positive	

CONSENT FORM

I Mr / Mrs / Miss / _____ have understood the procedure read by the Doctors. I in my whole conscious awareness give consent for the procedure. I understand that the procedure is done in good faith for the best therapeutic results possible. I fully understand the consequences of the procedure. I can resign from the study at any point of time.

Signature

Name :

Date and Time :

Signature of Researcher :

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Correlation of clinical,radiological, microbiological Features and drug resistance pattern of mycobacterium Tuberculosis in patients with HIV & Tuberculosis co-infection

Principal Investigator : Dr.V.Elakya

Designation : PG in MD (TB&RD)

Department : Department of TB&RD
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 08.04.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

24/9/13

MEMBER SECRETARY,
IEC, SMC, CHENNAI

Lin	ID	AGE	SEX	HEIGH	BMI	CONTACTHOTB	HIVSTAGE4	DISSEMINATEDTB	CD4COUN	SPUTUMSMEAR	LPA	CULTURE	CAVITATION	RU	RM	RL	LU	LM	LLZ	hiv	att	BMI	CXR	CONTACT	TB	SENSITIVITY PATTERN	TB CASE	SPUTUMSCOR	sympto	CD4COU	scorin	hivtreatment
1	7255032005	37	FEMAL	1.54	15.6	No	Yes	No	21	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	Yes	Yes	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	4	on ART
2	928072013	34	MALE	1.65	15.43	No	No	No	122	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	3	not on ART
3	37102002	37	MALE	1.67	14.3425723	No	No	No	231	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	4	not on ART
4	2139012014	65	MALE	1.55	18.73	No	No	No	134	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	365	1	1	not on ART
5	1625062013	40	MALE	1.55	17.8980229	No	No	No	509	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	120	0	2	not on ART
6	5596022008	32	FEMAL	1.54	20.661157	No	No	No	413	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	2	0	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	3	on ART
7	240062008	33	MALE	1.74	16.51	No	No	No	146	SCANTY	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	Yes	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	30	1	4	not on ART
8	1565092013	24	MALE	1.56	16.4365549	No	No	No	374	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	0	2	not on ART
9	10052012	38	MALE	1.57	15.82	No	No	No	153	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	1	5	on ART
10	2799062013	39	MALE	1.56	16.025641	No	Yes	No	241	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	1	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	15	0	4	on ART
11	5179032002	37	MALE	1.69	16.1058786	No	No	No	218	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	4	on ART
12	114112013	48	MALE	1.56	20.96	No	No	No	59	2+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	Yes	No	No	No	Yes	No	0	0	0	0	0	0	RESISTANT TO H	NEW	1	15	1	2	not on ART
13	853062003	56	MALE	1.64	15.62	No	No	No	157	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	30	1	4	on ART
14	330032013	33	MALE	1.65	13.96	No	No	No	7	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	3	on ART
15	2605122013	60	MALE	1.63	13.93	No	No	No	234	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	0	1	not on ART
16	1280112005	48	MALE	1.62	15.24	No	No	No	75	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	Yes	Yes	No	No	No	Yes	No	0	2	1	1	0	0	RESISTANT TO H	RETREATMEN	1	7	1	6	on ART
17	1774062004	39	MALE	1.64	13.01	Yes	Yes	Yes	13	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	Yes	1	0	1	0	2	1	SENSITIVE TO H ,R	NEW	1	30	1	7	not on ART
18	11122013	52	MALE	1.53	17.09	No	No	No	117	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	3	not on ART
19	2449012012	54	FEMAL	1.58	14.02	No	No	No	87	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	1	5	on ART
20	1328122013	37	FEMAL	1.6	15.63	No	No	No	208	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	Yes	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	30	0	1	not on ART
21	2788022014	36	MALE	1.64	13.01	No	No	No	535	NEGATIVE	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	Yes	Yes	No	Yes	Yes	No	0	2	1	0	0	0	RESISTANT TO H	RETREATMEN	0	90	0	3	not on ART
22	1746122013	37	MALE	1.71	16.76	No	No	No	82	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	7	1	3	not on ART
23	2935072006	33	MALE	1.69	17.86	No	No	No	766	SCANTY	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	No	Yes	Yes	No	No	Yes	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	7	0	5	on ART
24	743072013	58	MALE	1.64	16.73	Yes	No	No	388	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	0	30	0	3	not on ART
25	1288052013	35	MALE	1.65	16.8962351	No	No	No	18	3+	4 - MDR	4-MDR	No	No	No	No	No	Yes	No	0	0	1	0	0	0	MDR	NEW	1	90	1	3	not on ART
26	3390102013	28	MALE	1.63	13.55	No	No	No	84	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	180	1	3	on ART
27	4310052006	43	MALE	1.58	11.62	No	No	No	369	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	365	0	4	on ART
28	1854062013	28	MALE	1.6	16.8	No	No	No	169	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	90	1	2	not on ART
29	1948022014	45	MALE	1.64	16.36	No	No	No	78	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	7	1	3	not on ART
30	2852112013	40	MALE	1.5	15.56	No	No	No	25	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	120	1	3	not on ART
31	375022014	40	MALE	1.59	18.2	No	No	No	489	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	540	0	1	on ART
32	2288032013	46	MALE	1.6	14.84	No	Yes	No	43	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	1	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	14	1	6	on ART
33	571712004	53	MALE	1.59	14.239943	No	No	No	38	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	No	No	No	Yes	Yes	No	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	15	1	6	on ART
34	313062013	37	MALE	1.62	20.58	No	No	No	13	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	2	not on ART
35	1147112013	31	MALE	1.57	12.58	No	No	No	280	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	120	0	3	not on ART
36	3146122013	49	MALE	1.65	13.96	No	Yes	Yes	144	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	7	1	4	on ART
37	2737112013	53	FEMAL	1.5	13.33	No	No	No	187	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	3	not on ART
38	1953012007	36	MALE	1.7	15.57	No	No	No	110	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	180	1	5	not on ART
39	2964082010	48	MALE	1.57	13.3879671	No	No	No	250	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	30	0	3	not on ART
40	1764012014	37	MALE	1.62	14.86	Yes	Yes	No	184	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	No	No	No	1	2	1	0	2	0	SENSITIVE TO H ,R	RETREATMEN	1	30	1	8	not on ART
41	418042013	50	MALE	1.58	16.0230732	No	Yes	No	391	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	90	0	2	not on ART
42	5917072004	33	FEMAL	1.59	17.01	No	Yes	Yes	223	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	1	7	0	6	not on ART
43	405603213	27	MALE	1.7	17.3010381	No	Yes	Yes	120	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	Yes	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	10	1	5	not on ART
44	2121052009	32	FEMAL	1.52	10.39	Yes	No	No	66	3+	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	No	Yes	Yes	Yes	Yes	No	No	0	2	1	0	2	0	RESISTANT TO R	RETREATMEN	1	90	1	7	on ART
45	3468092013	50	MALE	1.66	15.97	No	Yes	No	40	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	4	not on ART
46	158022014	46	MALE	1.61	13.5	No	No	No	341	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	0	4	on ART
47	2620022013	36	FEMAL	1.58	15.62	No	Yes	Yes	8	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	1	90	1	7	on ART
48	3644022014	35	MALE	1.6	16.41	No	Yes	Yes	122	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	0	2	1	6	on ART
49	816022014	29	MALE	1.77	12.77	No	Yes	No	56	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	Yes	Yes	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	4	not on ART
50	3004052004	32	MALE	1.72	19.61	No	No	No	150	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	7	1	1	not on ART
51	2039022014	44	MALE	1.6	13.67	No	No	No	247	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	5	0	3	on ART
52	2335122013	49	MALE	1.69	14.0051119	No	No	No	425	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	No	Yes	Yes	No	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	60	0	5	not on ART
53	6162082004	38	FEMAL	1.55	12.07	No	Yes	No	125	NEGATIVE	0 -SMEAR NEGATIVE	4-MDR	No	No	Yes	No	No	No	No	1	2	1	0	0	0	MDR	RETREATMEN	0	180	1	5	on ART
54	916122005	46	MALE	1.69	16.1058786	No	Yes	Yes	255	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	1	7	0	6	on ART
55	1099062002	18	MALE	1.67	16.14	No	No	No	569	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0		0	1	on ART
56	677082013	48	FEMAL	1.54	25.3	No	No	No	338	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	0	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0		0	2	on ART
57	5827062005	36	MALE	1.64	15.6157049	No	Yes	Yes	336	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	0	3	0	5	on ART
58	1903072013	31	MALE	1.62	18.67	Yes	No	No	146	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	0	0	2	0	0	SENSITIVE TO H ,R	NEW	0	60	1	3	not on ART
59	3102004	33	MALE	1.7	15.92	No	No	No	101	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0		1	4	on ART
60	2286082013	29	MALE	1.63	15.06	No	Yes	Yes	237	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	42	0	3	not on ART
61	3713032013	36	MALE	1.69	15.0554953	No	Yes	Yes	42	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	7	1	4	not on ART
62	334032014	30	MALE	1.69	14.0051119	No	Yes	Yes	233	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	90	0	4	on ART
63	3003052013	40	MALE	1.68	14.17	No	No	No	197	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	90	1	4	on ART
64	820032002	53	MALE	1.65	16.16	No	Yes	Yes	119	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	0	10	1	6	on ART
65	4685112008	51	MALE	1.65	16.53	No	Yes	Yes	46	2+	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	No	No	No	Yes	No	No	No	1	2	1	0	0	1	RESISTANT TO R	RETREATMEN	1	90	1	7	on ART
66	5070012008	39	MALE	1.62	18.29	No	No	No	189	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	Yes	No	No	0	2	0	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	15	1	5	on ART

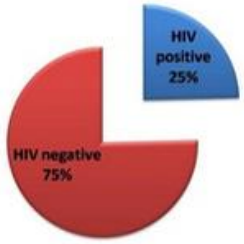
67	2395032012	36	MALE	1.63	15.4315179	No	No	No	295	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	60	0	4	not on ART
68	162112011	35	FEMAL	1.54	18.974532	Yes	Yes	Yes	371	NEGATIVE	0 -SMEAR NEGATIVE	3-RESISTANT TO R ALONE	No	No	No	Yes	No	Yes	No	1	2	0	0	2	1	RESISTANT TO R	RETREATMEN	0	30	0	6	on ART
69	4581012007	41	MALE	1.65	13.22	No	No	No	785	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	7	0	4	on ART
70	334102013	28	FEMAL	1.59	13.45	No	Yes	Yes	35	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	Yes	No	Yes	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	30	1	5	not on ART
71	3068022014	38	MALE	1.62	15.24	No	No	No	323	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	4	on ART
72	7131052007	45	MALE	1.59	17.7999288	No	No	No	28	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	1	5	on ART
73	746022014	30	MALE	1.57	15.82	No	No	No	521	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	0	2	not on ART
74	2142012012	32	MALE	1.6	12.890625	No	No	No	203	NEGATIVE	0 -SMEAR NEGATIVE	2-RESISTANT TO H ALONE	No	No	No	No	Yes	No	No	0	0	1	0	0	0	RESISTANT TO H	NEW	0	10	0	1	on ART
75	112112001	46	MALE	1.69	14.0051119	No	Yes	No	179	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	1	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	1	6	on ART
76	1782052008	37	MALE	1.62	16.38	No	No	No	227	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	7	0	3	on ART
77	2988122011	34	MALE	1.65	14.33	No	Yes	No	145	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	0	60	1	6	on ART
78	2590012013	39	MALE	1.68	14.17	No	No	No	93	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	30	1	4	on ART
79	2957012014	41	MALE	1.57	13.39	No	No	No	158	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	20	1	5	not on ART
80	3205012014	51	MALE	1.56	16.44	No	No	No	13	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	3	not on ART
81	2737102013	47	MALE	1.65	17.63	No	No	No	454	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	4	not on ART
82	166092009	43	MALE	1.54	18.97	No	No	No	35	3+	4 - MDR	4-MDR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0	2	0	1	0	0	MDR	RETREATMEN	1	180	1	5	on ART
83	2306112013	37	MALE	1.64	14.13	No	No	No	138	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	No	Yes	Yes	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	30	1	4	not on ART
84	3936032013	32	FEMAL	1.53	14.95	No	No	No	149	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	90	1	2	not on ART
85	2966102013	45	MALE	1.64	20.4491374	No	No	No	429	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	Yes	Yes	Yes	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	20	0	1	not on ART
86	1850062013	20	MALE	1.62	11.4311843	No	No	No	162	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	1	2	not on ART
87	774112013	38	MALE	1.61	11.57	Yes	Yes	No	55	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	1	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	90	1	6	not on ART
88	2474062013	55	MALE	1.58	16.42	No	No	No	116	NEGATIVE	0 -SMEAR NEGATIVE	2-RESISTANT TO H ALONE	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	RESISTANT TO H	NEW	0	14	1	2	not on ART
89	1003012014	40	MALE	1.56	18.49	No	Yes	No	126	NEGATIVE	0 -SMEAR NEGATIVE	2-RESISTANT TO H ALONE	No	No	No	Yes	No	No	No	1	0	0	0	0	0	RESISTANT TO H	NEW	0	90	1	2	not on ART
90	455042013	40	MALE	1.66	16.3303818	No	No	No	308	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	0	2	not on ART
91	2346102013	45	FEMAL	1.53	16.66	No	Yes	Yes	310	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	Yes	Yes	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	30	0	3	not on ART
92	2736092013	45	MALE	1.6	14.84	No	No	No	142	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	30	1	4	on ART
93	3868082009	40	MALE	1.68	15.94	No	No	No	299	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	5	0	4	on ART
94	3320122013	45	FEMAL	1.49	18.02	No	Yes	Yes	51	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	No	Yes	No	No	Yes	No	1	0	0	0	0	1	RESISTANT TO H	NEW	1	60	1	4	not on ART
95	2084052013	40	MALE	1.58	12.82	No	Yes	Yes	94	3+	4 - MDR	4-MDR	No	Yes	Yes	No	No	No	No	1	2	1	0	0	1	MDR	RETREATMEN	1	90	1	7	not on ART
96	1502082013	41	MALE	1.64	12.64	No	No	No	123	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	3	not on ART
97	1865012014	40	MALE	1.63	16.18	No	No	No	648	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	20	0	2	not on ART
98	134082007	43	MALE	1.67	13.98	No	No	No	67	NEGATIVE	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	Yes	Yes	No	No	No	No	No	0	2	1	1	0	0	RESISTANT TO R	RETREATMEN	0	10	1	5	on ART
99	136112013	27	MALE	1.59	15.82	No	No	No	92	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	90	1	2	not on ART
100	1404082012	45	MALE	1.68	14.88	No	No	No	72	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	1	5	on ART
101	1749062013	24	MALE	1.55	20.4	No	Yes	Yes	164	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	1	0	0	0	0	1	SENSITIVE TO H ,R	NEW	0	120	1	3	not on ART
102	993012007	36	MALE	1.69	16.1058786	No	No	No	313	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	0	2	not on ART
103	1592012013	30	MALE	1.62	17.1467764	No	Yes	Yes	39	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	No	No	Yes	No	No	No	1	2	1	0	0	1	RESISTANT TO H	RETREATMEN	1	120	1	7	on ART
104	3566012013	35	FEMAL	1.62	19.43	No	No	No	116	3+	4 - MDR	4-MDR	No	No	No	Yes	Yes	No	No	0	2	0	0	0	0	MDR	RETREATMEN	1	180	1	4	on ART
105	638062013	35	MALE	1.72	12.17	No	Yes	Yes	111	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	90	1	5	not on ART
106	2309082013	29	MALE	1.59	13.45	No	No	No	197	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	Yes	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	1	6	on ART
107	2983092013	32	MALE	1.64	16.7311124	No	No	No	131	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	10	1	3	not on ART
108	2284122013	40	MALE	1.65	12.86	No	Yes	Yes	258	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	60	0	3	on ART
109	2799122013	44	MALE	1.65	18.7327824	No	Yes	Yes	13	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	No	1	0	0	0	0	1	SENSITIVE TO H ,R	NEW	1	20	1	4	not on ART
110	43012014	31	MALE	1.65	14.69	Yes	No	No	33	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	120	1	5	not on ART
111	529122013	50	MALE	1.67	14.34	No	No	No	109	3+	0 -SMEAR NEGATIVE	3-RESISTANT TO R ALONE	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	RESISTANT TO R	NEW	1	45	1	3	not on ART
112	1049022014	37	MALE	1.64	17.85	No	No	No	133	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	Yes	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	14	1	3	on ART
113	320042013	35	MALE	1.59	15.8221589	No	No	No	244	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	Yes	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	0	2	not on ART
114	2400032014	43	MALE	1.65	15.79	No	Yes	No	159	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	1	3	not on ART
115	65042013	27	FEMAL	1.65	14.6923783	No	No	No	218	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	7	0	1	not on ART
116	4905062004	29	FEMAL	1.56	14.79	No	No	No	156	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	Yes	No	No	No	No	No	0	2	1	0	0	0	RESISTANT TO H	RETREATMEN	1	6	1	5	on ART
117	3499092003	45	MALE	1.63	18.07	No	No	No	235	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	90	0	0	on ART
118	1220082011	55	MALE	1.51	17.104513	No	No	No	514	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	14	0	4	not on ART
119	1594012014	58	MALE	1.56	16.4365549	No	No	No	694	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	14	0	2	not on ART
120	2514062013	30	MALE	1.49	18.47	No	No	No	512	NEGATIVE	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	Yes	No	No	No	Yes	No	No	0	2	0	1	0	0	RESISTANT TO R	RETREATMEN	0	90	0	3	not on ART
121	911072013	49	MALE	1.65	16.53	No	No	No	232	3+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	365	0	4	not on ART
122	518102012	26	MALE	1.69	14.3552397	No	Yes	Yes	168	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	30	1	4	on ART
123	4664082010	43	MALE	1.62	15.24	No	No	No	265	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	20	0	4	not on ART
124	385032014	49	MALE	1.64	14.87	Yes	No	No	251	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	No	Yes	Yes	No	Yes	No	0	0	1	1	2	0	SENSITIVE TO H ,R	NEW	1	180	0	5	not on ART
125	894012009	40	MALE	1.63	15.43	No	Yes	Yes	25	1+	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	No	No	No	Yes	Yes	No	No	1	0	1	0	0	1	RESISTANT TO R	NEW	1	60	1	5	not on ART
126	966022014	32	MALE	1.67	15.78	No	No	No	230	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	0	2	not on ART
127	3546012006	47	MALE	1.67	17.21	No	No	No	39	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	3	not on ART
128	2886082008	32	FEMAL	1.46	16.4195909	No	No	No	923	NEGATIVE	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	No	No	Yes	Yes	No	No	No	0	2	1	0	0	0	RESISTANT TO R	RETREATMEN	0	10	0	3	on ART
129	1040122012	36	MALE	1.57	17.44	No	No	No	42	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	60	1	5	on ART
130	2650052013	29	MALE	1.72	16.563007	No	Yes	Yes	85	NEGATIVE	0 -SMEAR NEGATIVE	4-MDR	No	No	No	No	No	No	No	1	0	1	0	0	1	MDR	NEW	0	14	1	4	not on ART
131	724062013	41	FEMAL	1.5	15.56	No	Yes	No	132	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	1	3	not on ART
132	1762072013	35	MALE	1.62	17.53	No	No	No	18	NEGATIVE	0 -SMEAR NEGATIVE	2-RESISTANT TO H ALONE	No	No	No	No	No	Yes	No	0	2	1	0	0	0	RESISTANT TO H	RETREATMEN	0	14	1	4	on ART
133	454042013	55	MALE	1.57	12.58	No	No	No	85	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	180	1	3	not on ART

134	3466042013	55	FEMAL	1.58	14.02	No	No	No	109	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	3	not on ART
135	3369122013	54	MALE	1.67	19.721037	No	Yes	Yes	124	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	0	0	0	0	1	SENSITIVE TO H ,R	NEW	0	10	1	3	on ART
136	875052013	40	MALE	1.42	32.24	No	No	No	104	NEGATIVE	0 -SMEAR NEGATIVE	2-RESISTANT TO H ALONE	No	No	No	No	Yes	No	No	0	2	0	0	0	0	RESISTANT TO H	RETREATMEN	0	15	1	3	on ART
137	3.4081E+10	43	MALE	1.56	14.38	Yes	No	No	95	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	60	1	5	not on ART
138	3245032013	33	MALE	1.59	13.8443891	No	Yes	Yes	75	3+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	120	1	5	not on ART
139	1132052013	35	MALE	1.55	15.4	Yes	No	No	199	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	Yes	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	3	1	5	on ART
140	527032009	40	MALE	1.67	15.78	No	Yes	No	269	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	Yes	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	15	0	3	on ART
141	2926062013	56	MALE	1.6	13.67	No	No	No	72	SCANTY	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	90	1	4	not on ART
142	2206062006	42	MALE	1.62	19.0519738	No	No	No	341	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1		0	1	not on ART
143	2709032014	40	MALE	1.7	15.92	No	No	No	102	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	3	on ART
144	2917032013	39	MALE	1.58	16.82	No	No	No	166	3+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	90	1	4	not on ART
145	475122013	38	MALE	1.61	13.89	No	No	No	107	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	365	1	3	not on ART
146	607122013	37	MALE	1.6	15.63	No	No	No	22	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	3	on ART
147	113112013	25	MALE	1.74	19.1570881	No	Yes	Yes	178	NEGATIVE	0 -SMEAR NEGATIVE	4-MDR	No	No	No	Yes	No	No	No	1	0	0	0	0	1	MDR	NEW	0	30	1	3	not on ART
148	3666032013	45	MALE	1.61	15.43	No	No	No	94	SCANTY	0 -SMEAR NEGATIVE	4-MDR	No	Yes	Yes	No	Yes	Yes	No	0	0	1	0	0	0	MDR	NEW	1	180	1	3	not on ART
149	3636032013	42	MALE	1.58	20.03	No	No	No	20	3+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	2	not on ART
150	3368122013	44	MALE	1.7	20.07	No	No	No	335	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	14	0	1	on ART
151	1638092009	45	MALE	1.7	10.38	No	No	No	111	3+	4 - MDR	4-MDR	No	Yes	Yes	Yes	Yes	Yes	No	0	2	1	0	0	0	MDR	RETREATMEN	1	90	1	5	on ART
152	2498122013	41	MALE	1.52	15.148892	No	Yes	No	26	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	Yes	No	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	4	not on ART
153	2491012014	35	FEMAL	1.62	15.241579	No	No	No	246	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	120	0	2	not on ART
154	3252072004	44	FEMAL	1.61	16.97	No	No	No	215	1+	4 - MDR	4-MDR	No	No	Yes	No	Yes	No	No	0	2	1	0	0	0	MDR	RETREATMEN	1	30	0	4	on ART
155	3881062011	56	MALE	1.66	19.6	No	No	No	105	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	7	1	1	on ART
156	2345052013	34	MALE	1.68	14.17	Yes	No	No	215	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	Yes	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	60	0	4	not on ART
157	464082013	38	MALE	1.67	12.91	No	Yes	Yes	120	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	Yes	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	1	10	1	5	not on ART
158	1135092103	41	MALE	1.6	13.67	No	No	No	254	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	0	2	on ART
159	193022013	41	MALE	1.58	16.02	No	No	No	256	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	90	0	3	on ART
160	2598062013	38	MALE	1.6	15.63	No	Yes	No	234	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	Yes	No	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	0	3	not on ART
161	2715072013	45	FEMAL	1.48	13.7	No	Yes	No	265	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	Yes	Yes	No	Yes	Yes	No	No	1	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	0	60	0	5	on ART
162	1984032014	26	MALE	1.64	13.01	No	No	No	123	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	120	1	2	not on ART
163	1720092013	40	MALE	1.65	18.37	Yes	No	No	79	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	0	2	0	0	SENSITIVE TO H ,R	NEW	0	3	1	3	not on ART
164	379122013	38	MALE	1.6	13.67	No	No	No	119	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	15	1	3	not on ART
165	1637052012	35	MALE	1.65	15.43	No	No	No	126	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	5	1	2	on ART
166	1614072013	44	MALE	1.66	16.33	No	No	No	33	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	14	1	2	on ART
167	2101042011	27	MALE	1.65	12.855831	No	Yes	Yes	123	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	No	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	1	15	1	7	on ART
168	1535062013	39	MALE	1.6	19.53	No	No	No	163	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	120	1	1	not on ART
169	1135032004	41	MALE	1.6	14.06	No	No	No	580	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	Yes	Yes	No	No	No	No	0	2	1	0	0	0	RESISTANT TO H	RETREATMEN	1	60	0	4	on ART
170	2323082009	31	MALE	1.54	15.6	No	No	No	87	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	20	1	2	not on ART
171	1376062013	33	MALE	1.71	14.36	No	No	No	10	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	180	1	3	on ART
172	3506112013	28	MALE	1.58	14.02	No	No	No	60	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	45	1	2	not on ART
173	3240012014	26	MALE	1.56	14.79	No	Yes	Yes	58	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	No	No	Yes	No	No	No	1	0	1	1	0	1	SENSITIVE TO H ,R	NEW	1	45	1	6	not on ART
174	1232122013	40	MALE	1.63	14.68	No	No	No	28	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	7	1	3	not on ART
175	1071022014	40	MALE	1.63	16.18	No	Yes	Yes	37	NEGATIVE	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	No	No	Yes	No	No	No	1	0	1	0	0	1	RESISTANT TO H	NEW	0	30	1	4	not on ART
176	4555062007	37	MALE	1.6	17.58	No	No	No	241	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	Yes	No	No	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	3	0	5	on ART
177	1281012004	40	MALE	1.6	13.67	No	No	No	28	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	3	not on ART
178	2810032009	32	MALE	1.65	16.1616162	No	No	No	204	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	7	0	4	on ART
179	3862042009	49	MALE	1.68	17.7154195	No	No	No	391	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	No	No	No	No	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	90	0	3	not on ART
180	346102013	45	MALE	1.55	13.32	No	No	No	331	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	10	0	1	not on ART
181	82122013	52	MALE	1.55	15.82	No	No	No	298	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	30	0	3	not on ART
182	5015042007	52	FEMAL	1.52	17.31	No	No	No	124	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	30	1	2	not on ART
183	2495012014	23	MALE	1.7	15.57	No	Yes	Yes	117	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	7	1	4	on ART
184	5799032006	46	MALE	1.68	14.17	No	Yes	Yes	132	3+	4 - MDR	4-MDR	No	No	Yes	No	No	No	No	1	2	1	0	0	1	MDR	RETREATMEN	1	30	1	7	on ART
185	790092013	55	MALE	1.65	13.59	Yes	Yes	Yes	455	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	1	0	1	0	2	1	SENSITIVE TO H ,R	NEW	1	90	0	6	not on ART
186	3559032013	30	MALE	1.62	14.48	No	No	No	190	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	3	not on ART
187	2387022012	33	MALE	1.64	13.01	No	No	No	237	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	No	Yes	No	Yes	Yes	No	0	2	1	1	0	0	SENSITIVE TO H ,R	RETREATMEN	1	7	0	5	on ART
188	1.2771E+10	41	MALE	1.62	16	No	No	No	255	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	7	0	1	not on ART
189	4311092004	40	MALE	1.68	14.17	No	No	No	180	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	15	1	5	on ART
190	1893102012	40	MALE	1.69	14.71	No	No	No	175	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	No	No	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	90	1	5	not on ART
191	2852082013	42	MALE	1.71	14.36	Yes	No	No	323	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	2	0	SENSITIVE TO H ,R	NEW	1	30	0	4	not on ART
192	3350102013	32	MALE	1.72	14.53	No	No	No	106	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	30	1	2	not on ART
193	4864082010	29	MALE	1.69	16.11	No	No	No	120	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	15	1	5	on ART
194	224022014	37	MALE	1.43	21.52	No	No	No	61	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	2	not on ART
195	856082010	36	MALE	1.8	13.89	No	No	No	122	1+	2- RESISTANT TO H ALONE	2-RESISTANT TO H ALONE	No	No	No	No	Yes	No	Yes	0	0	1	0	0	0	RESISTANT TO H	NEW	1	30	1	3	on ART
196	1897092013	33	MALE	1.64	18.96	No	No	No	326	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	Yes	Yes	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	7	0	1	not on ART
197	1456092013	47	MALE	1.62	15.24	No	No	No	334	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	Yes	Yes	Yes	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	180	0	3	not on ART
198	3534052006	47	MALE	1.61	16.2	No	No	No	223	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	30	0	2	not on ART
199	3895052006	44	MALE	1.61	13.5	No	No	No	289	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	3	0	1	on ART
200	3615022012	21	FEMAL	1.55	14.57	No	Yes	Yes	278	2+	3- RESISTANT TO R ALONE	3-RESISTANT TO R ALONE	No	Yes	No	No	Yes	No	No	1	2	1	0	0	1	RESISTANT TO R	RETREATMEN	1	60	0	6	on ART

201	3670122013	44	MALE	1.72	20.96	No	No	No	16	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	2	not on ART
202	2879022014	55	MALE	1.7	17.99	No	Yes	No	348	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	Yes	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	180	0	3	not on ART
203	3185022014	45	MALE	1.59	15.031051	No	No	No	248	3+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	60	0	2	not on ART
204	150102013	33	FEMAL	1.54	16.87	No	Yes	Yes	152	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	Yes	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	30	1	4	not on ART
205	2487052013	45	MALE	1.64	17.1	No	Yes	Yes	38	SCANTY	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	1	2	1	0	0	1	SENSITIVE TO H ,R	RETREATMEN	1	30	1	7	on ART
206	1238012014	32	MALE	1.65	14.69	No	No	No	57	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	1	2	not on ART
207	3705022014	41	MALE	1.59	13.84	No	Yes	Yes	180	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	365	1	4	not on ART
208	1548032014	40	MALE	1.67	12.91	No	No	No	67	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	10	1	2	on ART
209	2267122013	42	MALE	1.72	19.27	No	Yes	No	92	NEGATIVE	0 -SMEAR NEGATIVE	3-RESISTANT TO R ALONE	No	No	No	No	No	No	Yes	1	0	0	0	0	0	RESISTANT TO R	NEW	0	90	1	2	not on ART
210	1878092013	49	MALE	1.67	15.059701	No	No	No	114	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	30	1	2	on ART
211	3169052013	31	MALE	1.62	17.15	No	No	No	133	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	No	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	1	2	not on ART
212	3132062013	45	FEMAL	1.49	15.77	No	No	No	42	NEGATIVE	0 -SMEAR NEGATIVE	3-RESISTANT TO R ALONE	Yes	No	No	Yes	No	No	No	0	0	1	1	0	0	RESISTANT TO R	NEW	0	30	1	3	not on ART
213	2230092013	46	MALE	1.61	17.3604413	No	No	No	127	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	180	1	3	not on ART
214	1175092013	43	FEMAL	1.58	14.02	No	No	No	239	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	Yes	No	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	30	0	3	on ART
215	1775062013	45	MALE	1.65	12.4885216	No	No	No	57	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	1	120	1	3	not on ART
216	516112013	36	MALE	1.46	14.07	No	No	No	162	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	No	Yes	0	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	365	1	2	not on ART
217	1652062013	30	FEMAL	1.51	17.5430902	No	Yes	Yes	116	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	No	No	No	No	No	1	0	1	0	0	1	SENSITIVE TO H ,R	NEW	0	20	1	4	not on ART
218	3826032013	48	FEMAL	1.49	18.02	No	No	No	5	1+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	No	No	Yes	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	30	1	2	not on ART
219	1149032014	29	MALE	1.65	14.69	No	No	No	322	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	Yes	No	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	21	0	4	on ART
220	1903022014	29	MALE	1.65	14.69	No	Yes	No	247	NEGATIVE	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	Yes	No	No	1	0	1	0	0	0	SENSITIVE TO H ,R	NEW	0	60	0	2	on ART
221	2997022005	33	MALE	1.57	19.47	No	No	No	19	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	90	1	2	not on ART
222	5113022009	28	MALE	1.62	19.81	No	No	No	18	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	1	60	1	2	not on ART
223	195072005	47	MALE	1.7	18.69	No	No	No	593	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	Yes	No	No	Yes	No	No	0	2	0	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	7	0	3	on ART
224	2144082013	22	MALE	1.6	13.28	No	No	No	234	2+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	Yes	Yes	Yes	No	Yes	Yes	No	0	0	1	1	0	0	SENSITIVE TO H ,R	NEW	1	15	0	3	not on ART
225	2374032014	33	FEMAL	1.46	18.3	No	No	No	24	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	No	Yes	No	No	Yes	0	0	0	0	0	0	SENSITIVE TO H ,R	NEW	0	7	1	1	not on ART
226	2027052010	58	MALE	1.58	16.82	No	Yes	No	383	1+	1- SENSITIVE TO H & R	1-SENSITIVE TO H & R	No	No	No	No	No	No	Yes	1	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	30	0	5	on ART
227	4236072010	43	MALE	1.61	19.2893793	No	Yes	No	48	1+	4 - MDR	4-MDR	No	Yes	No	Yes	No	No	No	1	0	0	0	0	0	MDR	NEW	1	90	1	3	not on ART
228	800012014	53	MALE	1.61	18.52	No	No	No	104	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	No	No	No	0	2	0	0	0	0	SENSITIVE TO H ,R	RETREATMEN	0	180	1	3	not on ART
229	847072013	45	MALE	1.6	19.140625	No	Yes	Yes	147	NEGATIVE	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	No	Yes	No	No	No	No	1	2	0	0	0	1	SENSITIVE TO H ,R	RETREATMEN	0	30	1	5	not on ART
230	5814012007	40	MALE	1.7	13.84	No	No	No	154	2+	0 -SMEAR NEGATIVE	1-SENSITIVE TO H & R	No	Yes	Yes	Yes	Yes	Yes	Yes	0	2	1	0	0	0	SENSITIVE TO H ,R	RETREATMEN	1	60	1	5	on ART

INTRODUCTION

Drug resistant tuberculosis is the biggest challenge in tuberculosis high prevalent countries. In 2012, there were an approximately 8.6 million incident tuberculosis(TB) cases and 1.3 million people lost their lives due to the disease[1]. Among these 1.3 million deaths, 3,20,000 were among people who were human immunodeficiency virus (HIV) positive[1]. Thus 24.6% of TB deaths occurred among HIV positive cases.



TB deaths in world

Among these deaths, 1,70,000 deaths were due to multidrug

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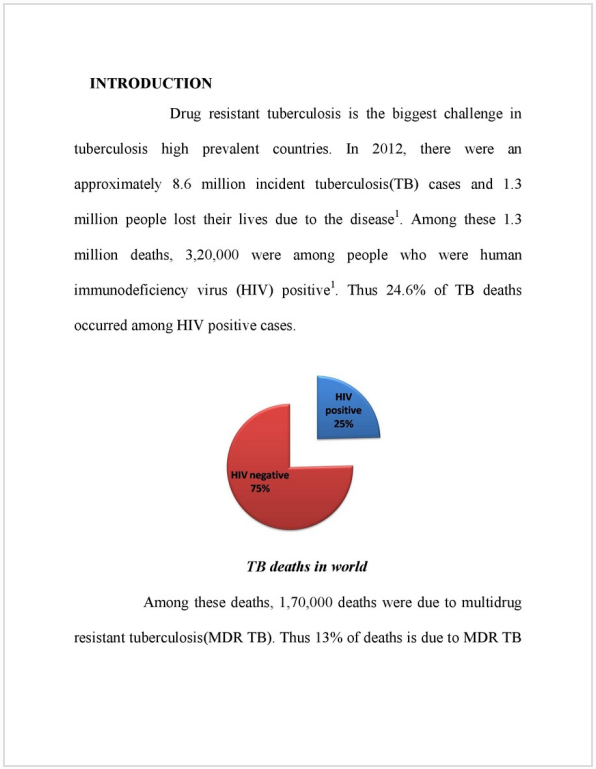

INTRODUCTION

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TB deaths in world

Among these deaths, 1,70,000 deaths were due to multidrug resistant tuberculosis(MDR TB). Thus 13% of deaths is due to MDR TB